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REGIONAL ENTERITIS

Report of Forty-Three Cases

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SINCE 1932, when Crohn, Ginzburg and Oppenheimer[1] awakened widespread interest in regional enteritis, there have been numerous reports of cases in the literature. Few of these have added much to the understanding of the disease. The clinical picture as originally described is still the only aspect of regional enteritis that is well understood. The pathology, diagnosis, prognosis and the most desirable treatment are as yet incompletely understood. The etiology is entirely obscure.

From 1930 to 1940, inclusive, 43 cases of regional enteritis were treated at the Massachusetts General Hospital, many of them on the private wards. This article deals chiefly with the results of the treatment of these cases.

CLINICAL PICTURE

Crohn and his associates[1] described four stages of regional enteritis: the acute (simulating appendicitis), the diarrheic, the obstructive and the fistulous. In the present series, at the time of admission, 6 cases were acute, 15 were diarrheic, 13 were obstructive, and 4 were fistulous. Five cases were encountered that represented a fifth, or symptomless, stage; most of these were discovered by x-ray at routine gastrointestinal study of symptoms that could not have been caused by regional ileitis. One case, however, was more definite. A pyloroplasty was performed for a proved duodenal ulcer, and at routine exploration of the abdomen a typical regional ileitis was found, both by palpation and by observation. This persisted and was confirmed later by x-ray study, but never caused any symptoms.

The 4 patients who presented themselves with intestinal fistulas had had previous operations. Two additional cases developed fistulas following operative procedures in this hospital. None of the cases developed fistulas without operation. It is accordingly apparent that the four classic stages of the disease are not necessarily consecutive. The fistulous stage often comes directly after the acute stage, usually following an appendectomy. This fact has been emphasized by Ginzburg.[2]

In the present series, as in those reported by others, regional enteritis was commonest in relatively young people, the average age being thirty, with extremes of fourteen and fifty-seven years. Yunich and Crohn[3] have recently reported the oldest case yet recorded, in a patient aged seventy. There is no predilection for race, since only 11 of our cases occurred in Hebrews, and although the ratio of females to males was 29:14, no constant sex predominance has been found in larger series.

In the 33 cases in which data on stools could be obtained, there were only 2 patients whose stools were positive for occult blood or who gave a history of bleeding. This low incidence of intestinal bleeding is in accordance with the experience of others but is surprising in view of the fact that mucosal ulcerations are such a characteristic part of the pathology of the disease.

In our series, the terminal ileum alone was involved in 27 cases; the terminal ileum and the cecum were the site of the lesion in 10 cases; and other areas of small bowel were involved in 6. Ravdin and Johnston,[4] in a survey of the literature, found that the site of the lesion was as follows: terminal ileum alone, 261 cases; terminal ileum and cecum, 100 cases; and other areas of the small bowel, 2 cases. Granulomatous processes in all parts of the gastrointestinal tract have been described.[5-7] Although several cases of unusual granulomatous inflammatory lesions primary in the stomach or colon have come to our attention, the pathologic findings have not been definite

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enough to warrant their addition to this series of cases.

Fissure or fistula in ano is a common accompaniment of regional enteritis, and 9 patients had had one or the other at some time in their lives. There is no implication that these lesions are a part of the primary pathologic process. It is rather to be supposed that they are secondary to irritating diarrhea, which so often occurs in ulcerative colitis. No interintestinal or intestinoperineal fistulas were encountered in this series, although such lesions have been described as not uncommon.[1]

Diagnosis

The diagnosis of regional ileitis is made in one or more of three ways: pathological examination, gross observation at the operating table, and x-ray study. In all the cases in our series, evidence of the disease was demonstrated by at least one of these methods. A diagnosis of regional ileitis was made by x-ray study in 16 of 30 cases that were later proved by operation; no definite x-ray diagnosis was made in 11 cases. In only 3 cases was the disease present when the involved region had appeared normal on x-ray examination. The four x-ray signs of Kantor[8]—the "string" sign, the filling defect in the terminal ileum, the dilated intestine above it, and the conical shape of the barium shadow—were of use in some of the advanced cases, but x-ray study was also helpful in many cases before these signs were evident. The so-called "motility" gastrointestinal series, with the taking of hourly plates to visualize the barium in the terminal ileum, was of the greatest value. We have not used the Miller–Abbott tube, as Boon[9] has done, to make the examination simpler, but this has definite points of merit, the chief of which is the ability to use, thereby, a much smaller amount of barium. We look forward to employing it in the future when the occasion arises. We are of the opinion that, whether or not disease is discovered by the gastrointestinal motility series in the terminal ileum, completeness demands that a barium enema be administered. One patient, who underwent a very radical resection of the right colon and lower ileum, had a prompt subsequent appearance of the disease in the left colon. It was not certain that the disease was absent in this area at the time of the original operation because a barium enema had not been given. A patient with regional ileitis deserves as complete a preoperative study of the intestinal tract as it is possible to give him.

Pathology

The typical pathologic picture of regional enteritis is that of a chronic granulomatous process in the intestinal wall and mesentery. Crohn, Ginzburg and Oppenheimer[1] considered the disease a pathologic entity consisting of chronic inflammation that started in the serosal coat of the intestine and later involved the mucosa in edema, ulcers and pseudopolyps. The mesentery partakes in the edema, so that the mesenteric fat enlarges and apparently creeps up onto the intestinal wall, giving the impression that the intestine has sunk into its mesentery. Many observers, however, have regarded it as a nonspecific process from the pathological viewpoint.[10, 11] The microscopic appearance, which consists in chronic inflammatory elements, fibroplasia, occasional giant cells and even epithelioid cells, could be caused by any bacterial agent or foreign body capable of producing low-grade inflammation, and in this sense, the picture is nonspecific. A considerable degree of uncertainty also envelops certain patients with fistulas in whom secondary infection so destroys the accustomed pathologic appearance that the diagnosis is made rather by the clinical behavior of the disease than by the appearance of the diseased tissue.[2] Hadfield[12] found only 13 of 20 cases of regional enteritis that presented characteristic giant-cell lesions. The histology in the early cases that are discovered at operation for acute appendicitis is also not clear, for few specimens of the intestine are available for study at this stage. In the patients who are seen in this stage and recover spontaneously, it will always be impossible to make an accurate diagnosis. Strongly supporting the belief that the pathologic features of the disease are difficult to define as an entity is the fact that during the last nine years, although hundreds of clinical articles have been written on the subject, pathological journals have been extremely silent concerning the disease. It is probable that further definition of this aspect of regional enteritis will await discovery of the etiologic agent.

Etiology

Lengthy discussions of the different theories concerning the etiology of the disease have been published.[4, 7] Although interesting suggestions are made by various authors, no one holds a strong brief for his own theory. Perhaps the most promising hope lies in the search for some agent that primarily obstructs the mesenteric lymphatics. Whether this is a lipoid,[10] some form of silica,[13] or a virus is entirely unknown. The similarity or relation of the disease to lymphogranuloma inguinale, to Johne's disease of cattle,[14, 15] to chronic dysentery,[16] to tuberculosis, to sprue[17] and to Boeck's sarcoidosis is interesting but uninformative.

Treatment

It was at first thought that, since regional enteritis was a specific disease affecting most commonly the terminal ileum, an area so amenable to successful surgical resection, surgery should be the therapeutic method of choice in all cases. It was soon realized, however, that many of the "early" cases either were not regional enteritis or underwent spontaneous regression. Therefore, the form of treatment that has been almost universally advocated has been surgical resection in all cases of the disease that were well established, but conservative therapy in the early, acute cases. The results of this policy are not easy to evaluate either in the cases reported in the literature or in those of our series. The length of the follow-up, the criteria for diagnosis, the stage and extent of the disease, and the magnitude of the resection performed are vital data but, unfortunately, are all too scant.

Table 1. *Results of Treatment in Cases Reported in the Literature.*

Author	Type of Treatment	Total No. of Cases	Patients Recovered or Improved	Patients Unimproved	Deaths in Hospital
Dixon[18]	Detour operation	14	5	5	4
	Resection	29	24	3	2
Crohn[19]	No operation	11	3	8	
	Operation		36	3	(10–15%)
Mixter[20]	Operation	278		(20%)	(14%)
Ravdin and Johnston[4]	Resection	88	60		
	Detour operation	290	89		
Cutler[14]	Resection	8	2	5	1

Table 1 gives a summary of the results of treatment in the significant series from the literature. There are four points of interest in this table: Dixon,[18] Crohn[19] and Mixter[20] all report 80 to 90 per cent of good results from resection; Cutler's poor results from resection form a sharp contrast to those of the first three authors, and are the basis for his advocating conservative treatment of all cases; the results from detour operation, or ileocolostomy, are not so good as those from resection; and the operative mortality from resection is about 15 per cent.

Table 2 presents an analysis of the cases at the Massachusetts General Hospital. It reveals the disturbing fact that, although 26 patients had resection* with only 1 operative death, only 6 of these were symptom free on follow-up inquiry, and only 2 more were not incapacitated by recurrence or persistence of symptoms. Of the 5 patients who had ileocolostomy or detour operations alone, 2 are well, and 3 died later. It is unfair to compare the ileocolostomy group with the resection group because the ileocolostomy often precedes the resection: in other words, if a patient has an ileocolostomy done and continues to have symptoms, but is not too sick for further surgery, a resection is usually performed. The only cases, therefore, that remain for analysis as "ileocolostomies" are those in which the patients got well or those in which they became worse and died. These factors should be taken into account when one considers the poorer results from detour operations as reported in the literature. It has recently been suggested that the reason ileocolostomy is unsuccessful in relieving symptoms is that most surgeons do it without transecting the ileum distal to the anastomosis and thus do not ensure complete diversion of the fecal stream from the diseased area. It is certainly logical to suppose that if ileocolostomy alone is to be done, the procedure should be performed in this manner. That this is not a cure-all, however, can be seen from Table 2, which shows that, of the 2 symptom-free patients, 1 had transection performed and 1 did not.

Table 2. *Results of Treatment in 43 Cases at the Massachusetts General Hospital.*

Type of Treatment	Total No. of Cases	Recovery	Persistence of Symptoms: No Incapacitation	Partial Incapacitation	Total Incapacitation	Deaths in Hospital	Deaths later
Resection	26						
First stage	16	2	1	5	6	1	1
Second stage	10	4	1	2	2	0	1
Detour operation	5						
Complete	4	1	0	0	0	0	3
Partial	1	1	0	0	0	0	0
Conservative	12	5	4	1	0	1	1
Totals	43	13	6	8	8	2	6

The same difficulty is realized if one compares the patients treated conservatively, in whom the results were excellent, with those treated surgically. The former group comprises, with 1 exception, patients in the acute and less established phase of

*Two patients had the original resection at other hospitals.

the disease. It is obvious that no conclusion can be drawn from conservative versus radical treatment in established regional enteritis unless alternating cases are treated by the two methods. The exception referred to above, however, is instructive. The patient was a thirty-year-old married woman who had suffered from diarrhea and inability to gain weight for six years. Her case was followed for two years. There was definite x-ray evidence of regional inflammation in the terminal 46 cm. of the ileum. This was the one patient in the partially incapacitated group who was conservatively treated. She is able to do all her housework except for occasional periods when she becomes slightly overtired or emotionally upset; the usual diarrhea of two or three stools a day then changes to six or seven a day for a week or so. This occurs approximately every three or four months. A recent x-ray film shows very slight progression of the disease. The patient presents a problem somewhat similar to many who have had unsuccessful reactions.

An attempt was made to analyze the individual cases treated by surgery with a view to finding an indication of why some of the operations were successful and some not. The three important recommendations made by most authors were kept especially in mind: to resect the diseased area, leaving a wide margin of normal intestine between it and the transection; to search for and remove "skip" areas; and to resect widely the involved mesentery and its lymph nodes. Since these 31 patients were operated on by eighteen different surgeons, there was no strict uniformity of operative treatment in this series, and the records of the operative procedures are not informative on the above topics. In 3 of the cases that were unimproved by resection, however, the definite statement is made that the resection was done well beyond the diseased intestine. A specific statement that skip areas were not present was not made, but since in each case the recurrences were in the region of the previous resection, it seems that, even had skip areas been present, they could not have been responsible for the recurrence. It is also confusing that 1 patient, who is now symptom free, presented himself with disease in the ileocecal region and in five skip areas elsewhere in the small intestine. Resection of the ileocecal region and only one of the skip areas was done, leaving four that have caused no trouble.

On the basis of these considerations, it seems that one must agree with Cutler about the low percentage of cures that surgery has to offer. We do not agree with him, however, that, because of this, the medical treatment of the established disease should replace the surgical. It is extremely rare that such patients become spontaneously symptom free as Moschowitz's[21] did. Resection offers a certain percentage — small, perhaps, but nonetheless definite — of cures, and should be advocated when an established case is first recognized as such. By more radical and careful operations and with consideration of the three recommendations of Crohn and Dixon, perhaps our results can be improved. In recurrent cases, it is logical to advocate reoperation only for symptoms that are crippling — namely, uncontrollable infection and obstruction. It is probable that mild or moderate diarrhea alone in these recurrent cases should not be cause for further surgery. Only 1 of 6 cures was the result of a reoperation.

Various specific forms of conservative treatment have been suggested, the chief of which are x-ray therapy and chemotherapy with the sulfonamide group of drugs. One patient, a young boy who died later in tetany, received x-ray treatment without avail when it was first known that his resection had been unsuccessful. We have had no experience with chemotherapy, having been discouraged by the unfavorable report of this form of treatment in one of Rhoads's[22] cases.

Prognosis

The prognosis when the disease is not cured by surgery is variable. The patient may fail rapidly, as those with overwhelming secondary infection and fecal fistulas most frequently do (2 patients in our series). There may be remissions, with many years of temporary relief between symptoms (4 cases). The course is most commonly slowly and progressively downward, with gradual weight loss, increase in diarrhea and x-ray evidence of larger areas of intestinal involvement (10 cases). Or the disease may remain, to all intents and purposes, stationary, without evidence of progression (5 cases).

Of the 2 deaths in the hospital, one was from malnutrition in the form of tetany in a young patient who had an acute, severe attack of diarrhea superimposed on a state of chronic, less severe diarrhea of several years' duration. The other patient had tetanic manifestations secondary to failure of calcium and vitamin D absorption; this was associated with failure of absorption of the other fat-soluble vitamins.[23] The deficiencies were controlled in this case by intensive vitamin therapy.

Six patients died following discharge from the hospital after the original operation. As in most diseases, death is the result of a complication rather than of the disease itself. The three complications that are to be feared are extensive infection, malnutrition and intestinal obstruction. Three of the 6 late deaths were from prolonged and extensive infection, which eventually

became uncontrolled. Another case presented vitamin K deficiency as part of the clinical picture. The 2 remaining patients who died after discharge left no clue concerning the cause of death. No patient died from intestinal obstruction per se. The slowly progressive development of obstruction in these cases and the infrequency of gangrene of the intestine result in a type of obstruction that is comparatively simple to deal with.

Summary and Conclusions

The clinical picture, diagnosis, pathology, etiology, treatment and prognosis of regional enteritis are discussed, and 43 cases are reported.

A fifth, or symptomless, stage of the disease is added to the four accepted stages.

The x-ray examination by the so-called "motility" intestinal series was of great help in diagnosis, being at fault in only 3 of 30 cases.

The pathologic picture is not that of a distinct entity.

The various theories concerning the etiology of the disease are mentioned.

The results of surgical resection in established cases in this series were not good, since there were satisfactory results in only 8 out of 26 cases.

Conservative treatment in early cases gave good results.

Since conservative treatment of the established disease, however, gives little hope of cure, radical resection should still be offered these patients as the initial procedure.

The ideal form of treatment of the disease will not be forthcoming until the etiologic agent is discovered.

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COLLES'S FRACTURE*

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A WORKING knowledge of Colles's fracture is essential because the injury is frequent and is often followed by impaired use of the hand and wrist. This fracture is usually caused by a fall on the outstretched hand.

Anatomy

The expanded lower end of the radius articulates with the carpal navicular and lunate below and with the ulnar head on the inner side. The head of the ulna is held against the sigmoid cavity of the radius by the pronator quadratus muscle and by the meniscus. The latter is attached to the lower margin of the sigmoid cavity and the base of the ulnar styloid. In addition, the two collateral ligaments are of importance in stabilizing the wrist. The lower radioulnar ligaments are taut only in the extremes of rotation, and the palmar and dorsal radiocarpal ligaments in extremes of flexion and extension.

Lying in close relation to the lower radius are the various tendons passing from the forearm to the wrist and hand. These tendons and the median nerve are liable either to laceration or to adhesions following the hemorrhage and edema that frequently accompany these fractures.

Pathology

Radius. The plane of fracture of the radius may be horizontal or oblique, single or comminuted. The whole lower extremity is sometimes shattered, with involvement of the lower articular surface. The commonest type of comminution is that of the dorsal surface. The details of the planes of fractures are significant from the standpoint of maintenance of reduction. After the patient has recovered from the anesthetic, the pull of the flexor and extensor muscles crowds the fragments together. If the plane of fracture is single and horizontal, this force aids in holding the fragments in place, but if it is oblique or comminuted the tendency is for the previous deformity to recur in spite of splints. In adolescents, the bone is apt to give way at the epiphyseal plate.

If displacement is present, the lower fragment may be shifted or tilted. In the former event, its axis remains parallel to that of the upper fragment; in the latter, it is angulated. Such displacement may occur in one of four directions: palmar, dorsal, radial or ulnar. Since the bone is cancellous, there is apt to be some crushing or impaction. Overriding rarely occurs. The most frequent condition found is a combination of dorsal shift and tilt and radial shift and impaction.

Ulna. In the majority of cases with displacement, the ulnar styloid is detached near its base because of the pull of the ulnar collateral ligament. Although it usually heals by fibrous rather than by bony union, this lesion is not serious.

Inferior radioulnar joint. This joint is intimately associated with pronation and supination, and its derangement may result in persistent pain or limitation of motion. With any shortening of the radius, the articular surfaces lose their proper relations. The meniscus is often torn. Rarely, an actual dislocation at this joint complicates the fracture.

Adjacent soft parts. With a backward displacement of an oblique fracture, the sharp jagged edge of the upper fragment can cause considerable damage to the lower fibers of the pronator quadratus muscle, the flexor tendons and even the median nerve. Rarely, the ulnar nerve may be injured. Injury to the short thumb extensors may result in subsequent rupture.

Associated injuries. Fracture of the navicular and luxation of the lunate are sometimes associated injuries.

Symptoms and Signs

The symptoms of the break are pain, which may be very mild at first, and weakness of the hand and wrist. Localized tenderness over the line of fracture can be elicited both directly and indirectly. If the patient is seen within a few minutes of injury, a narrow, sharply elevated transverse swelling will be noted on the dorsal surface at the site of fracture, because of hemorrhage. As the blood extravasates and edema ensues, the swelling extends and becomes less prominent. With the usual dorsal and radial shift of the lower fragment, the typical silver-fork deformity occurs. The normally flat dorsal surface of the lower forearm, wrist and hand then shows a distinct elevation. At the same time, the palmar concavity disappears. With any shortening of the radius, the relation of the two styloids is altered. Instead of being almost a centimeter lower, the radial styloid will be nearer the level of the ulnar. Normally, a line passing down the middle of the forearm follows the middle metacarpal and the middle finger. With a radial shift of the lower

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fragment, this line tends to follow the fourth metacarpal and ring finger. At the same time, the ulnar head becomes more prominent.

Examination

Examination should be made as gently as possible. With the story of a fall followed by pain and impairment of function, one should presume that a fracture exists until one can prove the contrary. Localized tenderness increases the probability. Actual deformity confirms the diagnosis of fracture with displacement. After a test for possible nerve injury, the examination is completed by x-ray films taken in two planes. In studying x-ray films, it is not enough to establish the primary diagnosis; other bone lesions should be looked for. The main problem, however, is to decide how the planes of fracture run and what displacement exists. Such evidence is needed to decide what maneuvers are necessary to reduce the displacement, what is required to maintain the reduction, how long immobilization is necessary and, lastly, what the probable outcome will be.

Treatment

Reduction. Any displacement of fragments should be corrected except under certain conditions. This requires an anesthetic, either local or general, not only to lessen pain but to reduce the amount of secondary trauma. All materials for immobilization should be assembled before the anesthetic is given. The essential principle in reduction of displacements is to disengage the fragments before trying to manipulate the lower one into place. This is accomplished by traction on the hand, countertraction being applied to the upper arm by an assistant or broad band fastened to the end of the table and the elbow being flexed to a right angle. Traction should be slow and gentle at first and gradually increased as necessary, aided perhaps by rocking of the lower fragment. After the fragments have been disengaged, the lower one can be swung and pushed into place. The exact maneuvers necessary should be planned according to the x-ray evidence. After reduction, the position should be checked under the fluoroscope.

Immobilization. The type of splint varies with the habits and desires of the surgeon. Some form of molded plaster splint is perhaps the favorite. I prefer the so-called "sugar-tong" splint, a single strip of plaster that starts in the palm opposite the metacarpal necks, passes up the palmar aspect of the forearm around the flexed elbow and down the dorsal aspect to the metacarpal heads. It is essential to allow free motion at the metacarpophalangeal and interphalangeal joints. As soon as the plaster has set and a bandage has been applied, post-reduction films should be taken, not only for the surgeon's information but also for his protection. After the swelling has subsided for seven to ten days, it may be wise to change to a circular plaster gauntlet from the midpalm to the upper forearm.

Too early removal of splints tends to prolong rather than shorten convalescence. If the splints allow free motion at the metacarpophalangeal and interphalangeal joints and the patient is made to keep his fingers moving, this not only will maintain range and power in these joints but by internal massage will help the circulation at the site of fracture and thus hasten union.

Treatment of different types. From the standpoint of treatment and prognosis, fractures of the lower radius can be divided into four main groups, with three minor types.

Fractures without displacement, of course, require no reduction and no anesthetic. After three or four weeks, the splints may be replaced by a leather wristlet. In such fractures, the patient should have complete return of function.

When *fractures with a single horizontal plane of fracture and slight or no impaction* are seen early, complete reduction should be possible. The muscle pull tends to hold the fragments in place, and the wrist can be put in a comfortable midposition. The period of immobilization needed is but little longer than that in the first group.

When *the plane of fracture is oblique* or when *there is comminution of the dorsal surface*, there is a strong tendency, because of the muscle pull, for the dorsal shift and tilt to recur. This can be partially overcome if the splint is applied with the wrist in strong flexion and moderate adduction. The position can be changed to a more comfortable one during the third week, but splints should be retained for five or six weeks.

There is a group of cases, perhaps 5 per cent, in which *the comminution is so extensive that no form of splint alone prevents collapse and shortening.* In this type, it is well worth while to use the double Kirschner wire and plaster method. One wire is passed through the second, third and fourth metacarpals near their base (the fifth is usually missed). A second wire is inserted higher in the forearm. At first, I used this wire through the radius a little above the middle, but experience has shown that it is better to place it in the upper ulna just distal to the coronoid. After the wires are in place and yoked, reduction is obtained by traction on the wires, with necessary molding. While this is held, a circular plaster is applied, incorporating the two wires. These are left in place for five to seven weeks.

In *very old patients*, it is often wiser to provide protection for a short period without reduction, active motion being started as soon as possible.

Occasionally, *loose fragments* of bone are displaced so as to lie amid the tendons either in front or behind. These should be removed as soon as union has become fairly firm.

Three types of *late disability* can be helped by operative treatment: in cases with persistent posterior shifting of the lower fragment, in which the flexor tendons rub against the sharp edge of the upper fragment, with marked interference with the handgrip, simple removal of the projection through a lateral approach restores the power; when there is derangement of the lower radio-ulnar joint from shortening of the radius, which interferes with rotation, the pain, disability and deformity of the prominent ulnar head can be relieved by a subperiosteal resection of the lower 2 cm. of the ulna; and in cases with marked dorsal tilt and shift requiring an osteotomy, as the lower fragment is swung forward into position, a triangular space is left that can be filled with the new callus from the dorsal surface — if the ulnar head needs resection, this bone can also be used to fill the vacancy.

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THE PHARMACODYNAMICS OF SULFADIAZINE IN MAN*

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SULFADIAZINE, an analogue of sulfapyridine, (2-sulfanilamido-pyrimidine) has recently been synthesized by Roblin and his associates.[1] Reports on its fate, mode of action, absorption and toxicity in animals[2, 3] and in man[4–7] have appeared. The present discussion deals with observations on its pharmacodynamics in man.

MATERIALS AND METHODS

Ninety-eight men with upper respiratory infections or convalescing from pneumonia were studied. The drug¶ was given orally, intravenously, subcutaneously, intramuscularly and rectally. Observations were made on the fate of single oral doses of 2, 3, and 5 gm. and with repeated doses of 1 gm. every four and every six hours. Intravenously, 5 gm. of sodium sulfadiazine dissolved in 50 cc. of sterile distilled water was injected within one to three minutes. Infusions of 500 or 1000 cc. of a 0.5 or 1.0 per cent solution of sodium sulfadiazine in sterile physiologic saline were given at the rate of 2.5 to 3.0 cc. per minute. Subcutaneously, 1000 cc. of a 0.5 per cent solution of sodium sulfadiazine in saline was administered over a period of two hours. Intramuscularly, 2 or 3 gm. of sodium sulfadiazine in 50 cc. of sterile distilled water was injected into the upper outer quadrant of the buttocks. Rectally, 5 gm. of sulfadiazine was given as a retention enema (starch). Determinations of free and total sulfadiazine in the blood were made at intervals of fifteen minutes for the first hour, at hourly intervals for the next five hours and at intervals of twenty-four hours until the blood showed negligible amounts. Collection and analysis of urine were continued until only traces were detected. The distribution of the drug was studied in the spinal, pleural and peritoneal fluids. The concentrations were determined by the method of Bratton and Marshall[8] by means of a photoelectric colorimeter.

ABSORPTION FROM GASTROINTESTINAL TRACT

Oral Administration

The sulfadiazine concentrations in the blood obtained after single oral doses of 2, 3 and 5 gm. are shown in Figure 1. At the end of four hours, single 2-gm. doses of sulfadiazine in 5 subjects resulted in blood levels of the free drug ranging from 2.0 to 3.5 mg. per 100 cc. Single 3-gm. doses given to 6 subjects yielded blood levels varying from 2.5 to 4.0 mg. per 100 cc. Seven subjects who received 5-gm. doses had concentrations of free sulfadiazine ranging from 3.6 to 5.5 mg. per 100 cc. In all cases, measurable quantities of the drug were found in the blood for seventy-two hours.

Multiple oral doses of sulfadiazine were administered to 40 subjects to determine and evaluate the blood concentrations obtainable with different dosage schedules. When statim doses of 2, 3, 4 and 5 gm. were followed by 1 gm. every four or six hours, day and night, it was found that those subjects who had received 4 or 5 gm. as an initial dose maintained slightly higher levels

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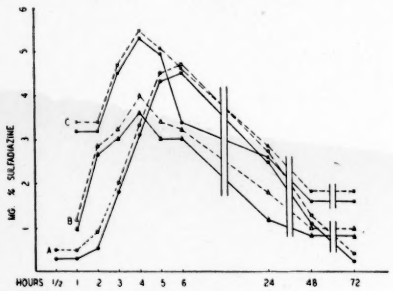
than those who had received the smaller doses. The levels, however, were maintained as well when the continued doses were given at intervals of four or six hours.

Rectal Administration

Following a retention enema containing 5 gm. of sulfadiazine, the concentration in the blood



	MG. SULFADIAZINE OUTPUT IN URINE HOURS	24	48	72	96	RECOVERY TOTAL	PER-CENT
A	FREE	943	242	39		1224	61.2
	CONJUGATED	21	111	25		157	7.8
	TOTAL	964	353	64		1381	69.0
	% CONJUGATED	2.2	31.4	39.1		11.4	
B	FREE	1032	165	61	41	1299	43.3
	CONJUGATED	770	131	42	4	947	31.5
	TOTAL	1802	296	103	45	2246	74.8
	% CONJUGATED	42.5	44.3	40.8	8.9	42.0	
C	FREE	873	362	143	56	1434	28.7
	CONJUGATED	291	282	105	51	729	14.6
	TOTAL	1164	644	248	107	2163	43.3
	% CONJUGATED	25.0	43.8	42.3	47.6	33.7	

FIGURE 1. *Sulfadiazine (Free and Total) Blood Concentrations and Urinary Excretions after Single Oral Doses of 2 (A), 3 (B) and 5 (C) Gm. of Sulfadiazine.*

was never above 1.0 mg. per 100 cc., but traces were detectable for seventy-two hours.

PARENTERAL ADMINISTRATION

Parenteral administration may be advisable because some patients cannot take the drug orally or an early high concentration is required. The available routes are intravenous, subcutaneous and intramuscular.

Intravenous Route

High concentrations were found immediately in all subjects receiving sodium sulfadiazine intravenously. Free sulfadiazine in the blood reached concentration peaks varying from 16 to 24 mg. per 100 cc. in ten to thirty minutes after injection of 5 gm. of the drug. The blood concentrations decreased gradually for the first six hours. This was followed by a more rapid decline for the next eighteen hours, and traces were detectable after forty-eight hours.

Because of the rapid drop in concentration following intravenous injection of the drug, an attempt was made to maintain high levels with a continuous slow infusion. A series of 8 subjects received infusions of 500 to 1000 cc. of a 0.5 or 1.0 per cent solution of sodium sulfadiazine at the rate of 2.5 to 3.0 cc. per minute. During the infusion, a steady increase in concentration occurred. Peaks ranged from 11.9 to 19.2 mg. of free sulfadiazine per 100 cc. The decline in concentration following the cessation of the infusion, although steep, was not so sharp as that following a rapid injection of the same amount of drug in greater

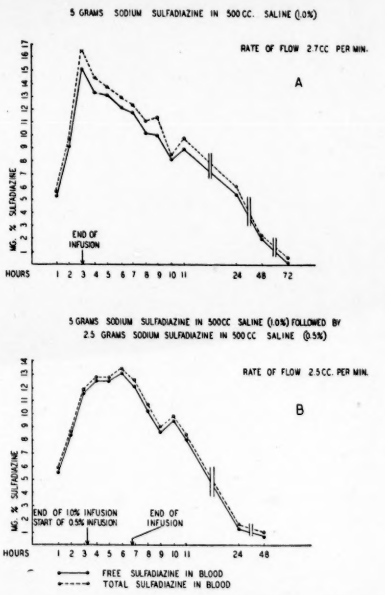

5 GRAMS SODIUM SULFADIAZINE IN 500 CC. SALINE (1.0%)
RATE OF FLOW 2.7 CC PER MIN.
A
MG. % SULFADIAZINE
END OF INFUSION
HOURS
5 GRAMS SODIUM SULFADIAZINE IN 500 CC SALINE (1.0%) FOLLOWED BY 2.5 GRAMS SODIUM SULFADIAZINE IN 500 CC SALINE (0.5%)
RATE OF FLOW 2.5 CC. PER MIN.
B
END OF 1.0% INFUSION
START OF 0.5% INFUSION
END OF INFUSION
FREE SULFADIAZINE IN BLOOD
TOTAL SULFADIAZINE IN BLOOD

FIGURE 2. *Sulfadiazine (Free and Total) Blood Concentrations (A and B), after Continuous Intravenous Infusion of Sodium Sulfadiazine, Using Solutions of Different Strengths.*

concentrations. Figure 2 shows representative curves.

In 1 subject, an initial infusion of 5 gm. of the sodium salt of the drug in 500 cc. of physiologic saline solution produced a blood concentration of

11.5 mg. per 100 cc. at the termination of the infusion (Fig. 2*B*). When this was immediately followed by 500 cc. of a 0.5 per cent solution at the same rate of flow, blood levels between 12 and 13 mg. per 100 cc. were maintained for the duration of the infusion (four hours). In another case, the initial infusion of 5 gm. sodium sulfadiazine in 1000 cc. of saline solution was followed by oral doses of 0.5 gm. every four hours. Concentrations between 9 and 11 mg. per 100 cc. were maintained.

Subcutaneous Route

Three subjects received 5 gm. of sodium sulfadiazine subcutaneously in 1000 cc. of physiologic saline solution; the hypodermoclysis required two hours. The highest concentration of the free sulfadiazine was reached in six hours, the peaks being 7.5, 7.8 and 8.2 mg. per 100 cc. respectively (Figure 3). The increase, as well as the drop, in

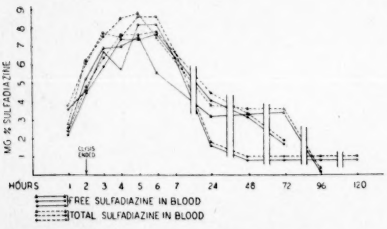

MG. % SULFADIAZINE
1 2 3 4 5 6 7 8 9
CLOTS ENDED
HOURS
1 2 3 4 5 6 7 24 48 72 96 120
FREE SULFADIAZINE IN BLOOD
TOTAL SULFADIAZINE IN BLOOD

FIGURE 3. *Sulfadiazine (Free and Total) Blood Concentrations Following Hypodermoclysis of 5 Gm. of Sodium Sulfadiazine in 1000 Cc. Saline Solution in 3 Patients.*

concentration was gradual, and in one subject a concentration of 1.0 mg. per 100 cc. was detectable at the end of one hundred and twenty hours.

Intramuscular Route

Two subjects were given 2 and 3 gm. of sodium sulfadiazine (in 50 cc. of sterile distilled water) intramuscularly in one minute. The pH of the solution was 9.5. The blood levels reached peaks of 6.2 and 8.5 mg. of free sulfadiazine per 100 cc., respectively, in one hour and dropped gradually (Fig. 4). The blood-level curves show a similarity to those obtained after intravenous injection.

CONJUGATION IN BLOOD

Conjugated sulfadiazine is present in small amounts in the blood. Different subjects showed only moderate variations in the quantity of conjugated sulfadiazine, and the quantities were small irrespective of the amount administered or its portal.

In 1 case, the conjugated sulfadiazine in the blood was markedly elevated. This patient was given a single dose of 5 gm. of sulfadiazine orally. Concentrations of the free and conjugated drug

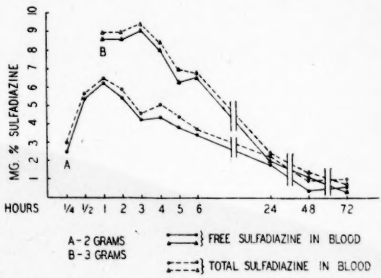

MG. % SULFADIAZINE
1 2 3 4 5 6 7 8 9 10
B
A
HOURS
¼ ½ 1 2 3 4 5 6 24 48 72
A - 2 GRAMS
B - 3 GRAMS
FREE SULFADIAZINE IN BLOOD
TOTAL SULFADIAZINE IN BLOOD

FIGURE 4. *Sulfadiazine (Free and Total) Blood Concentrations Resulting from Intramuscular Injections of 2 (A) and 3 (B) Gm. of Sodium Sulfadiazine in Distilled Water.*

were detectable seven days after it had been administered. At the end of ninety-six hours, the blood contained 5.3 mg. of the conjugated form per 100 cc. and 2.3 mg. of the free form. The urine in this case also showed an unusual output of conjugated sulfadiazine. The total recovery was 61.8 per cent, two thirds of which was conjugated. This subject had nephrosclerosis with azotemia (a blood creatinine of 6.0 and a blood urea nitrogen of 130 mg. per 100 cc.).

ELIMINATION

Discontinuance of administration is followed by early rapid excretion, which subsequently becomes slower. Sulfadiazine was observed in the urine within thirty minutes after oral administration, and immediately after intravenous injection. Within seventy-two hours, most of it had been eliminated. Approximately 50 per cent of the total amount recovered was excreted in the first twenty-four hours, and about 80 per cent in forty-eight hours. For as long as six days, both free and conjugated forms could be detected in measurable quantities in the urine.

The amount of sulfadiazine (free and conjugated) recovered from the urine varied from 30.4 to 94.5 per cent of the dose given, with an average of 60.5 per cent (Table 1). After oral administration, the recovery averaged 56.1 per cent, and after intravenous, intramuscular and subcutaneous administration, the average recovery was 69.7 per cent.

Generally, there was a lag of twenty-four hours in the appearance in the urine of the conjugated as compared with the free form. In most cases,

of the total amount recovered in the urine, about 35 per cent was excreted as conjugated sulfadiazine, with extremes of 11.4 and 71.4 per cent. Of the total amount of conjugated drug recovered, approximately 45 per cent was accounted for in the first twenty-four hours, and 75 per cent in the first forty-eight hours. The percentage of conjugated sulfadiazine excreted from day to day was approximately the same in all patients, irrespective of the duration of administration (Fig. 1). It appears that the rate of conjugation, as measured by urinary excretion, is a characteristic of the patient and does not depend on the amount of drug given or its route of administration.

TABLE 1. *Urinary Recovery of Sulfadiazine.*

PATIENT	ROUTE OF ADMINISTRATION	DOSE	AMOUNT RECOVERED			PERCENTAGE CONJUGATED (OF TOTAL RECOVERY)	PERCENTAGE RECOVERED		
			FREE	CONJUGATED	TOTAL		FREE	CONJUGATED	TOTAL
		gm.	*mg.*	*mg.*	*mg.*				
C. F.	Oral	2	1224	157	1381	11.4	61.2	7.8	69.0
G. A.	Oral	2	1292	609	1901	32.0	64.1	30.4	94.5
A. S.	Oral	3	442	1105	1547	71.4	14.7	36.8	51.5
J. B.	Oral	3	758	450	1208	37.2	25.2	15.0	40.2
C. F.	Oral	3	708	205	913	22.4	23.6	6.8	30.4
W. J.	Oral	3	1298	947	2245	42.2	43.3	31.6	74.9
T. H.	Oral	5	1274	972	2246	43.3	25.5	19.5	45.0
C. F.	Oral	5	1778	700	2478	28.3	35.5	14.0	49.5
O. S.	Oral	5	1006	2087	3093	67.4	20.1	41.8	61.9
D. D.	Oral	5	2047	1087	3134	34.7	40.9	21.7	62.6
G. E.	Oral	5	1434	729	2163	33.7	28.7	14.6	43.3
A. M.	Oral	11*	3701	1494	5195	28.7	33.7	13.6	47.3
M. C.	Oral	14*	5812	4783	10,595	45.1	41.5	34.2	75.7
W. B.	Oral	22*	2546	5673	8219	69.0	11.6	25.8	37.4
R. T.	Intravenous	5†	1873	497	2370	20.9	37.5	9.9	47.4
H. S.	Intravenous	5†	2294	804	3098	25.8	45.9	16.1	62.0
B. D.	Intravenous	7.5†	3415	896	4311	20.8	45.7	11.9	57.6
A. F.	Intramuscular	2†	1089	316	1405	22.5	54.4	15.8	70.2
F. H.	Intramuscular	3†	1918	878	2796	31.4	63.9	29.3	93.2
B. D.	Subcutaneous	5†	3038	1138	4176	27.2	60.7	22.8	83.5
A. W.	Subcutaneous	5†	2448	1241	3689	33.6	48.9	24.9	73.8

*Repeated doses.
†Sodium sulfadiazine.

DISTRIBUTION IN BODY FLUIDS

The drug may be detected in high concentrations in the spinal, pleural and peritoneal fluids. As indicated in Table 2, the spinal-fluid levels of free sulfadiazine varied from 56 to 95 per cent of the simultaneous blood levels. In some cases (M. L., R. L. and J. W.), a tendency to maintain a fairly constant relation to the blood levels was observed. In pleural fluid, collected without local anesthesia, the range was 54 to 132 per cent of the blood levels. In none of these, had the drug been injected into the pleural space. The possibility that the excretion of the drug from the pleural fluid into the blood is slower than its absorption from the blood is a probable explanation for the high pleural-fluid concentrations. In one subject (A. P.), following an intravenous injection of 5 gm. of sodium sulfadiazine, a concentration of 8 mg. of the free drug per 100 cc. was observed in the ascitic fluid in ten minutes. At the end of forty minutes, the concentration of the free drug was 21.3 mg. per 100 cc., as compared with 15.2 mg. in the blood.

DISTRIBUTION BETWEEN CELLS AND PLASMA

Several blood samples, at hourly intervals, were drawn from each of 6 subjects to study the distribution of the drug in blood cells and plasma. Approximately 80 per cent of the sulfadiazine was found in the plasma. There was no relation between the distribution and blood levels. The amounts of conjugated sulfadiazine were small in both cells and plasma.

SOLUBILITY

Sulfadiazine was found to vary in solubility with the medium employed. When the solubility of the drug was tested at 22°C. and at 37°C., it was found to be 9 and 12 mg. per 100 cc., respectively, in water, 13 and 19 mg. per 100 cc. in physiologic saline solution, and 136 and 204 mg. per 100 cc. in whole blood. In serum, at 22°C., it was soluble to the extent of 206 mg. per 100 cc.

TOXICITY

In the subjects reported herein and in a larger series (over 300 cases) to be reported, the incidence of toxic manifestations was relatively low. Nausea and vomiting occurred in 10 per cent of the cases. A morbilliform rash was seen in 3 patients, 1 of whom also had a moderately severe conjunctivitis. Blood changes and mental disturbances were not encountered. Crystals in the urine were less frequently observed than with the other drugs. In 1 case, at operation, crystals of sulfadiazine were present in the pleural fluid following an intrapleural injection of a solution of sodium sulfadia-

zine. Gross hematuria occurred on three occasions. In no case did albumin or casts appear in the urine as a result of the drug. Neither intramuscular nor subcutaneous injections produced any adverse local or general reactions. The high pH (9.5) of the solutions was apparently without harmful effects.

TABLE 2. *Relation of Free Sulfadiazine Concentrations in Spinal, Pleural and Peritoneal Fluids to Simultaneous Blood Levels.*

PATIENT	DAY OF TREATMENT	TOTAL DOSE	ROUTE OF ADMINISTRATION	TYPE OF FLUID	CONCENTRATION OF FREE SULFADIAZINE: BLOOD LEVEL	FLUID LEVEL	PERCENTAGE OF BLOOD LEVEL	DIAGNOSIS
		gm.			*mg./100 cc.*	*mg./100 cc.*		
M. B.	4	20	Intravenous	Spinal	33.6	22.6	67	Meningitis (pneumococcus, Type 14)
M. L.	3	10	Oral	Spinal	• 16.2	10.3	63	Meningococcal meningitis
	4	14		Spinal	16.2	9.1	56	
	5	20		Spinal	15.3	9.4	61	
	6	28.5		Spinal	17.6	11.4	65	
	9	53		Spinal	14.4	8.6	60	
J. S.	2	10	Oral	Spinal	6.7	4.2	63	Tuberculous meningitis
	4	18		Spinal	5.5	3.9	71	
F. J.	5	50	Intravenous and oral	Spinal	25.0	21.5	86	Meningitis (pneumococcus, Type 8)
D. S.	6	29	Oral	Spinal	7.3	6.6	90	Pneumonia (pneumococcus, Type 7)
R. L.	6	68	Intravenous and oral	Spinal	18.4	15.8	86	Meningitis (pneumococcus, Type 3)
	9	119		Spinal	28.2	23.0	81	
	10	119		Spinal	12.4	11.8	95	
J. W.	4	71	Intravenous and oral	Spinal	25.8	15.2	59	Meningitis (pneumococcus, Type 7)
	5	106		Spinal	27.8	20.6	74	
	8	202		Spinal	52.4	33.6	64	
E. J.	2	25	Oral	Spinal	28.8	24.2	84	Meningococcal meningitis
R. A.	4	20	Oral	Pleural	11.1	6.0	54	Lung abscess with empyema
C. F.	4	18	Oral	Pleural	2.9	1.9	65	Pneumonia (pneumococcus, Type 7) with sterile effusion
H. D.	4	23	Oral	Pleural	5.3	7.0	132	Pneumonia (pneumococcus, Type 7) with sterile effusion
S. N.	5	26	Oral	Pleural	5.7	6.5	114	Pneumonia (pneumococcus, Type 2) with sterile effusion
E. B.	4	21	Oral	Pleural	7.3	6.0	82	Lung abscess with empyema
L. W.	4	25	Oral	Pleural	13.6	15.3	112	Pneumonia (pneumococcus, Type 3) with sterile effusion
A. W.	7	43	Oral	Pleural	8.7	10.5	121	Empyema (pneumococcus, Type 7)
A. P.	1	5	Intravenous	Ascitic	15.2	21.2	140	Cirrhosis of liver

DISCUSSION

Sulfadiazine is readily absorbed from the gastrointestinal tract. Blood concentrations obtained are generally higher than those observed with similar doses of sulfapyridine and sulfathiazole. The drug disappears from the blood more slowly than either of these. The amount conjugated in the blood is less than that with sulfapyridine or sulfathiazole. The conjugated fraction in blood and urine does not increase with continued administration. In the urine, about a third is found to be conjugated, although in exceptional cases a much larger proportion may be excreted in this form. Rapid urinary excretion of the drug may account for the small quantities of conjugated sulfadiazine in the blood.

When both rapid attainment and maintenance of high blood levels are desirable and oral administration is not feasible, the intravenous infusion of sodium sulfadiazine is practical. Blood concentration may be varied either by adjustment of the concentration of the infusion liquid or by regulation of the rate of flow. Although the immediate levels obtained with the slow infusion method are somewhat lower than those obtained with the rapid intravenous injection of a similar dose, a high concentration is more readily maintained. This method is safe, flexible and efficacious.

Sulfadiazine is widely and readily distributed in body fluids. It penetrates well into the pleural and peritoneal cavities. Concentrations in the spinal fluid are usually about two thirds those of the simultaneous blood levels.

With initial doses of 2, 3, 4 and 5 gm. followed by 1 gm. every six hours, levels are obtained that are similar to those reached when the drug is given every four hours. Blood concentrations are independent of the total dose and the dose per kilogram of body weight.

The incidence of toxic reactions is less with sulfadiazine than with sulfapyridine and sulfathiazole. When reactions occur, they are mild.

CONCLUSIONS

Sulfadiazine is readily absorbed from the gastrointestinal tract.

High levels may be obtained by several routes, but a rapid attainment and maintenance of high

blood levels is best accomplished with continuous slow infusion.

The amount of conjugated sulfadiazine in the blood is small, usually less than 20 per cent.

Although the amount of conjugated sulfadiazine excreted in the urine varies in different subjects, approximately 35 per cent is excreted in this form.

The drug diffuses well into the body fluids.

The ratio of spinal-fluid to blood concentration appears to be constant.

Toxic manifestations of sulfadiazine are less frequent and milder than those noted with sulfapyridine and sulfathiazole.

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UNUNITED HIP FRACTURES*

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BOSTON

During the last decade or so, surgeons have concentrated on the initial reduction, fixation and aftercare of fresh fractures of the femoral neck. As a result, the percentage of good end results typified by solid union and painless functioning has markedly increased. However, as I[1] contended in 1940, when I had occasion to discuss the problem of ununited hip fractures, ununited femoral-neck fractures, including many of the nonfunctioning, painful types, still occur. To render the limb painless and functioning, some type of reconstructive (or as the late Dr. F. J. Cotton tersely put it, "destructive") type of operation is required.

Methods

Various types of reconstructive procedures for these cases of nonunion have evolved. But I still believe that the following five methods form a good armamentarium for the surgeon attempting to do such work: the Colonna[2] (a modification of the Whitman[3]); the Magnuson[4] (a modification of the Brackett[5]); the various bone-stimulating operations—direct grafting, chip grafts, peg grafts and hole drilling; the fusion operation; and the simple oblique McMurray[6] osteotomy method. Since my views on the first four methods have not changed radically during the last two years, I quote below what I had to say of them at that time.

The fifth, the McMurray method, I practically passed over because up to that time my experience with it had been short and unsatisfactory. Since then, I have done such osteotomies in 8 cases, with gratifying end results in 6. The remaining 2 patients were treated too recently for the ultimate outcome to be judged; all that I can say about them is that to date they are progressing well. My experience with the method during the last two years has impressed me very favorably with its simplicity, its wide adaptability and its promise of a high rate of good end results and of a return to normalcy.

To offer a basis of comparison between methods, I shall review the operative procedure of the first four methods and my evaluation of them, as I gave them in the previous paper, with some very minor revisions. Following this, I shall consider the McMurray oblique osteotomy.

The Colonna type of reconstruction consists in: sectioning close to their insertions of all muscles attached to the region of the greater trochanter, with preservation of a thin layer of fibromuscular tissue over the upper end of the bone; removal of the head; placing of the upper extremity of the femur deeply and firmly within the acetabulum, transplantation of the gluteus medius and minimus group of muscles downward on the shaft of the femur as far as they will reach, and the secure fastening of them to the bone; after wound repair and dressing, application of a plaster-of-Paris spica with the leg in 20 to 30° abduction; at the end of four weeks, cutting away of the lower posterior half of the cast in the affected leg so as to allow knee flexion several times a day; removal of the entire cast in the sixth week, placing of the leg in a special type of foot sling hitched to a Balkan frame, and institution of a special series

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of exercises; and use of crutches at the eighth week and direct weight bearing one to two weeks, or more, later, depending on the individual case.

The essentials of the Magnuson[4] method (a modification of the Brackett method) are: exposure by the Smith-Petersen or the Callahan approach; removal of fibrous tissues between the fractured ends, followed by a test to ascertain whether the head is viable or nonviable; hollowing of the head in the form of a cone, pointing upward and slightly backward; rotation of the femur inward and, with a thin-bladed chisel, removal of the trochanter in a line sloping from the base of the neck of the shaft; rounding of the end of the shaft in the same curve as that in which the head has been hollowed out; abduction of the leg so that the upper end of the shaft may be pried into the head; reattachment of the trochanter to the shaft on the cut surface so that it is moved downward and outward and held in that position by heavy silk ligatures; application of a plaster-of-Paris spica, which is retained for eight to twelve weeks, occasionally longer in my experience (that is, until bony union has taken place); removal of the spica, the legs being kept in some abduction, however; finally, periodic clinical examinations and check-up roentgenograms to determine when actual direct weight bearing can be started.

The various direct bone-grafting, pegging and hole-drilling methods, I believe, need not be described, since they are so varied. Suffice it to say that when I decide to use such a procedure I combine several. These operations are followed by plaster-of-Paris spica fixation for ten to fourteen weeks, or until union has been established, and then by the use of crutches and protective ambulatory splints until definite firm union has been obtained.

The hip-fusion method is generally performed by means of Hibbs's procedure, or with some modification, when the head of the femur must be removed or is useless. In these cases, Cotton[7] combined Hibbs's fusion operation with Albee's old plan of squaring. Following the operation, a plaster-of-Paris spica is applied and retained until fusion is established. As a rule, this takes twelve to sixteen weeks. A walking spica is then applied, or if fusion is firm, a protective ambulatory splint and crutches or crutches alone are used. No direct weight bearing is permitted until union has been firmly established clinically and roentgenographically.

Dr. Charles H. Bradford,[8] who is with the American Hospital in England, describes a hip-fusion method that is being worked out by Dr. Britten, who does the equivalent of a McMurray osteotomy, slides the shaft inward and lays a wide solid piece of tibial graft above it like a roof, firmly set in the chiseled groove in the ischium just below the acetabulum. Dr. Bradford considers this type of arthrodesis to be a revolutionary development that may replace all other forms of hip fusion. I mention it because I consider it much simpler and basically sounder than the prevalent hip-fusion methods.

The McMurray[6] osteotomy is a bifurcation operation based on the suggestion of Lorenz[9] in which the shaft of the femur is transferred directly under the lower margin of the acetabulum and head of the femur. The chief purpose of this operation is to change a shearing force into a direct one. The following are the steps in the procedure: a 15-cm. incision is made along the lateral side of the upper end of the femur in the trochanteric area; the fracture site is exposed so as to place the osteotomy line accurately; an oblique osteotomy is performed, beginning on the outer side of the shaft, generally about the lower end of the greater trochanter, and ending above the tip of the lesser trochanter; the upper end of the shaft of the femur is pried and shoved inward until the cut end is under the acetabulum and femoral head —this is followed by repair of the wound; a plaster-of-Paris fixation is used for a period long enough to ensure union at the site of the osteotomy (varying in my cases from eight to fourteen weeks). This fixation of the limb is in the neutral position in very slight abduction, to prevent the development of knock-knee following removal of the plaster cast. McMurray asserts the objection that this protracted fixation by plaster spica is likely to be followed by troublesome rigidity, especially if the knee joint does not hold, since in that event there is no torsion of the limb and consequently no continued strain on the joint, which lies comfortably in neutral, slight flexion position.

McMurray warns that the osteotomy should not be carried out on too high a level because the shaft of the femur cannot then be put under the head and acetabulum. Also, if the osteotomy is done at too low a level, no weight is borne directly through the shaft of the femur, so that the strain at the site of nonunion remains unaltered. The obliquity of the osteotomy makes more certain that union occurs between the fragments. McMurray further stresses the value of the correct position of the transferred shaft under the acetabulum and femoral head, the union between the divided fragments of the femoral shaft and the position of slight abduction, to prevent the development of a subsequent knee deformity.

Results

Of 12 cases treated by the Colonna method, what may be called good end results were obtained in 8. The patient must be a good operative risk for this procedure. The chronologic age need not be a deterring factor. The patient must, in the surgeon's judgment, be able to withstand a good amount of surgical trauma. The fracture site should show definite absorption of the femoral neck or head; the less femoral neck remaining, the easier the operation and the better the result. This method can also be considered in cases in which the head of the femur is dead. Arthritic changes in the hip are not conducive to a good result with this type of reconstruction, and therefore rule out this operation.

The following facts were noted in the 8 cases treated successfully by the Colonna method. The bed and hospital confinement was shorter than that by any of the other methods used. The average was six weeks in bed; the patients spent another two weeks up and about the ward before discharge. Patients left the hospital under their own power with the aid of a crutch or cane, depending on their confidence and readjustment ability. The average shortening in these cases was less than 2.5 cm.: 1.9 cm. in 3 cases, 2.5 cm. in 4, and 3.8 cm. in 1. This shortening was of no material consequence; it could be corrected by a slightly raised heel. Internal and external rotations at the hip were quite limited; abduction ranged from 25 to 45°, and adduction from 20 to 25°. The flexion at the hip was good, and extension was normal. Patients could stand alone on either leg. They had painless hips and could walk ordinary distances without fatigue or discomfort, although with a slight limp. They had, however, some social and physical discomforts. They complained of inability to put stocking and shoe on the affected leg, and protracted sitting, such as that at the card table or the theater, caused a sense of stiffening and discomfort in the affected hip.

To arrive at this result, the patient must go through a fair amount of severe surgical trauma, but the period of hip and leg fixation is comparatively short, as are bed confinement and hospitalization, which are important items when one knows, as in other procedures, what prolonged fixation and bed treatment will do to a patient locally and generally. This period of immobilization is also a significant factor from an economic standpoint, which today is the concern of both patient and hospital.

Of 7 cases in which the Magnuson operation was employed, good end results were obtained in 4. This method should not be considered in cases complicated by arthritic changes, or by any suspicion of cartilage degeneration or irregularity, or in cases in which the head of the femur is dead. I also believe that in ununited fractures of over one year's duration, or in cases in which no femoral neck is left, the patients are poor risks for this operation. In my experience, this procedure requires a very careful selection of cases. It involves somewhat more surgical trauma than the Colonna method. The fixation of the hip and leg and the bed confinement were quite long in these cases — ten to sixteen weeks. The patients left the hospital from the end of the tenth to the eighteenth week, under their own power and using crutches or an ambulatory Thomas splint and cane. They were bearing direct weight on the affected hips from the sixth to the ninth month. At that time, there was solid union of the reconstructed neck and head, and the hip joint was 90 per cent and more normal — as nearly normal as one could expect from a reconstruction.

The poor results in 2 cases were unfortunate. Neither fracture united. There was absorption at the reconstructed site soon after the operation. Both patients were over sixty years of age, chronologically and physically. The ununited fractures were of twelve and sixteen months' duration. One of these patients has since died, and the other is up and about as a crutch invalid but has a painless hip.

These cases have caused me to avoid the Magnuson method in ununited fractures of over twelve months' duration and in elderly people. Two of the successful cases were also benefited by these failures in that I not only chose them more carefully but, in addition to the reconstruction, did Bozsan's[10] hole drilling and crammed in some bone chips at the reconstruction site.

Bone grafting and allied methods were employed in 3 cases. The selection of ununited hip fractures for bone grafting, bone chips and hole drilling must be made early and with due care to the general condition of the patients, who must be above average physically to withstand successfully the prolonged spica and bed confinement. The femoral heads should be in good condition, and some of the neck should remain. Here again, those patients with arthritic changes or tendencies, or with any joint irregularity, should not be selected for these procedures.

In the 3 successful cases, the ununited fractures were of six and a half to eight months' duration. The femoral heads were all in good condition, and a fair amount of femoral neck remained. In 1 case, a simple, thorough cleaning out of the fibrous tissue between the head and neck was done, and the resulting gap was crammed

with bone chips. The 2 others had not only the hole drilling, as advocated by Bozsan, but also inlay grafts and bone chips. In these cases, spica fixation was maintained from twelve to sixteen weeks, and hospitalization lasted fourteen to eighteen weeks. All these patients left the hospital wearing protective ambulatory splints and using either a crutch or a cane. The time of direct weight bearing averaged from six to eight months. The knee joints in the affected legs in 2 of these patients lengthened the convalescence and delayed return to normalcy. The third patient had limited knee motion at operation, and this limitation persisted. The hips in the 3 patients had practically normal range of function, which was better than that in the successful Magnuson cases.

The simplicity, ease and nonshocking quality of these allied methods impressed me markedly and made me aware that early recognition of nonunion and early decision to use stimulating therapy should be sought.

The hip-fusion operation was performed in 3 cases. This method has been employed only in those ununited cases in which definite arthritic or other joint changes are shown. Again, my experience is limited, but it has been most satisfactory. Successful end results were obtained in 2 cases, and in another a successful outcome followed a secondary stimulation.

Of course, the successful end result is a stiff hip with social and physical discomforts very similar to those after a good Colonna end result— t least, that is how I have viewed it. To attain this result, the patient must go through severe surgery and a protracted spica fixation and hospitalization, varying from twelve to sixteen weeks. These are serious factors that one must face before selecting such a procedure, which is so tempting because the percentage of failures following its use is lower than that for any of the other present-day methods.

At the Boston City Hospital, 8 ununited hip fractures have been reconstructed by the McMurray osteotomy. Of these, 2 have been done too recently for the result to be judged. Five of the remaining 6 cases have gone to clinically good end results, and 1 patient, although not an absolute failure, still has to use crutches after six months. This simple osteotomy method obviously entails less surgical trauma than the other methods and, hence, less surgical shock. Thus, some cases that are deemed poor surgical risks for the Colonna, Magnuson or fusion operation may qualify for the McMurray method. However, the last is not well adapted to the following types of cases: those in which the femoral head is disintegrating; those in which the femoral neck has been absorbed and the shaft is riding high; and those in which the nonunion is not too old and the absorption has not progressed too far and in which a simple local bone-stimulating, or the Magnuson, operation seems indicated. Successful end results by these methods give almost 100 per cent return to normalcy and have stood the test of time, which may change some present thoughts on the McMurray osteotomy.

In the few cases done by this method at our hospital, the following data have been gathered: the patients have plaster-of-Paris spica fixation from eight to fourteen weeks, and hospitalization from ten to about seventeen weeks; they generally leave the hospital using crutches but soon thereafter omit them and use only a cane, with a good clinical end result; they still use a cane in going up stairs, limp slightly, but have no local hip pain or tenderness on walking, sitting or lying down; the shortening varies from 2.2 to 2.6 cm.; there is a limited degree of internal, but a good degree of external rotation at the reconstructed hip, and also a good abduction and adduction range; there may be occasional local stiffness; the patients can dress themselves in normal fashion, cross their knees and sit for protracted periods with ease and comfort. In short, a good 80 to 85 per cent return to normalcy is usually obtained.

At present the McMurray osteotomy seems adaptable to a greater variety of the painful ununited femoral-neck fractures than the other methods. The other points in its favor are its simplicity of execution, the production of less surgical shock and, lastly, the fairly high rate of good end results showing a very creditable percentage of return to normalcy.

However, I am still firmly convinced that if an unmistakable diagnosis of nonunion could be made in the early months following the initial reduction and fixation, more of the simple bone-stimulating or Magnuson operations could be performed. I also believe that the Colonna method still has a place in cases in which there has been much degeneration of the head or considerable absorption of the neck, with the shaft consequently riding high.

The fusion operation (possibly of the Britten type) should be reserved for the failures of the other methods and for the markedly arthritic types. I hesitate to do fusion in the very old, because of their extreme slowness to adapt themselves to the limitations of a stiff hip.

* * *

In conclusion, I must emphasize the fact that although each method described has its distinct uses and advantages,—the McMurray probably more than any of the others,—what I said in 1940

still holds true: there is no universal method of reconstruction of painful ununited femoral-neck fractures; I agree with Brackett's[5] statement that the surgeon's choice of procedure is still paramount.

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MEDICAL PROGRESS

SURGERY OF THE AUTONOMIC NERVOUS SYSTEM

Method of Study, with Particular Reference to the Interpretation of Clinical Results

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TO determine the effect of autonomic nervous activity on the peripheral circulation, in both health and disease, as well as before and after operations on the sympathetic nervous system, various methods of study are available. Some involve simple tests, such as surface-temperature determinations. More complicated measurements not available to all, such as those by the plethysmographic method, are frequently used. By this procedure, the number of cubic centimeters of blood passing through a unit volume of tissue per minute can be determined. Autonomic nervous impulses that are capable of modifying peripheral blood flow can be temporarily interrupted by procaine hydrochloride block. Thus, sympathetic pathways to the blood vessels of the extremities can be inactivated by the injection of the proper segments of the sympathetic trunk paravertebrally, by peripheral-nerve block or by spinal anesthesia. The last, of course, applies only to the legs. Other methods of inhibiting vasoconstriction, such as heating the trunk to promote reflex vasodilation, can be used. Of particular concern are the vasoconstrictor pathways, with which man is so abundantly supplied. These are active under many everyday circumstances, as in response to cold, pain, emotion and the upright position. When activated, the sympathetic nervous system greatly reduces circulation to the extremities, as well as to the viscera, both in the presence and in the absence of vascular disease.

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The state of activity of the autonomic nervous system is very dependent on environmental temperature. For this reason, controlled room-temperature conditions are essential to a study of patients both before and after operation. If the patient is placed in a *cool* environment for a given period, with a minimum of the body surface covered, vasoconstriction is induced. The surface temperature of an extremity is then measured, or the quantity of blood flowing through a given segment is determined by the plethysmographic method. The vasoconstrictor fibers are then temporarily interrupted by one of the methods mentioned, and the surface temperature or quantitative blood flow is again estimated. One can thus tell fairly accurately how much the circulation can be increased after sympathectomy. Certain exceptions to this statement need not be discussed at this point. It is essential that the same conditions of study be used in subsequent observations.

When patients are studied in a *warm* environment, vasoconstriction is not induced, and may be totally absent; in fact, in higher temperature ranges, vasodilation may actually be present. Under such conditions of study, the circulation of the extremities is not primarily dependent on vasoconstrictor activity. When judged in this manner, the blood flow to the skin and subcutaneous tissues after acute denervation by procaine hydrochloride block or actual surgical excision of the sympathetic nervous system may not be significantly altered. In fact, the maximal blood flow to an extremity is somewhat decreased by sympathectomy because vasodilator, as well as vasoconstrictor, fibers are interrupted.

Thus, if one compares the surface temperature of a denervated extremity and a normally innervated extremity after exercise or after the trunk has been heated to promote reflex vasodilation in the extremities, the normally innervated extremity is the warmer. The circulation of the sympathectomized hand is nevertheless high and adequate. If, then, the patient is again observed in a cool environment, or if while he is still in a warm environment, stimuli are utilized that generally invoke vasoconstriction, such as a loud noise, immersion of an opposite extremity in cold water, or an unpleasant thought, the findings are quite different. The denervated extremity maintains its high blood-flow level, whereas the circulation of the undenervated extremity generally is greatly decreased. Operations on the sympathetic nervous system, therefore, do not increase blood flow beyond its maximal level; they stabilize blood flow near and somewhat below this point. Because the action of the autonomic nervous system in the everyday life of the average person is preponderantly in the direction of vasoconstriction, the net result of inhibiting this mechanism is an increase in blood flow to the part.

This point may be more clearly illustrated by the case of a young woman who suffered from Raynaud's disease. I had occasion to sympathectomize one of her upper extremities before she went to Europe to compete as a member of the American Olympic Ski Team. Under virtually all circumstances, the denervated hand was much the warmer. The only exception was noted after the patient had climbed to the top of the course, which required considerable physical effort. At this point, the undenervated hand was the warmer. It was also pink and moist. The denervated hand, however, was also warm and of good color, and dry. At the same time, the body was uncomfortably warm, and conditions for reflex vasodilation were present. By the time that she reached the bottom of the incline and the end of a race, however, the undenervated hand was cold and ischemic whereas the denervated hand was warm and of good color, as before the race. At this point, the body was chilled, and together with the excitement associated with the event, conditions inducing vasoconstriction were present. There was no question whatsoever in her mind concerning which hand had the better circulation day in and day out, and needless to state, the other extremity was subsequently denervated.

When, on the other hand, one is dealing with impaired circulation in the presence of known organic vascular disease, the ability of blood vessels to relax in the acutely denervated state may be already lost. In many cases, their ability to constrict in response to nervous impulses is still preserved and can be abolished by proper surgical maneuvers. It therefore becomes increasingly imperative to stabilize blood flow at the highest possible level. That this may result in a striking increase in circulation, even in the presence of extensive obliterative vascular disease, is clear, provided one studies the patient before operation under conditions when vasoconstriction exists, and duplicates the same conditions for postoperative comparison. This seems to me to be the crux of the situation, and it is important enough to warrant a specific illustration.

Figure 1 presents the surface-temperature charts of a sixty-one-year-old man who was known to have peripheral arteriosclerosis, with obliteration of main-vessel pulsation below the femoral artery of one extremity. The other extremity also had calcified vessels, but main-vessel obliteration did not exist. Intermittent claudication of moderate severity was present in the more affected leg. After exposure of all four extremities for one hour at a room temperature of 68°F., with the patient in the horizontal position, and the body covered only by a sheet and a thin cotton blanket from axilla to groin, surface-temperature readings were taken. These were recorded at numerous points from the tip of the toe to the groin, as illustrated. The nature of the surface-temperature curves of the two extremities was similar in the undenervated state. There was no significant difference, in spite of the obvious difference in main-vessel pulsation. This type of curve, in which the surface temperatures began to fall from a high point in the extremity to the tip of a digit, indicates an unusual degree of vasospasm in response to environment. It is seen in both the presence and the absence of organic vascular disease. It is to be contrasted with surface-temperature levels in other patients with and without obvious vascular disease, in which cooling of consequence under the same conditions of study is confined chiefly to the distal portion of the foot or even to the digits only. This matter was recently discussed in greater detail.[1]

After exposure for one hour, the vessels of the lower extremity were acutely denervated by induction of spinal anesthesia with ensuing complete motor and sensory paralysis extending to the midthoracic level. The response of the two extremities was quite different. The surface temperatures of the extremity without main-vessel obliteration rose in a far more significant fashion, particularly in the more distal portions of the leg. On the more affected side, the surface temperature of the tip of the digit rose 5°F., and at the base, only 2°F. This was accompanied by im-

provement in color, the extremity being pink and dry by contrast with the cold, cyanotic, moist state of the tissues associated with collapsed veins and clinical signs of vasospasm, which existed in the undenervated state. These findings, together with the nature of the surface-temperature chart, indicated a worth-while result from sympathectomy in the more affected leg. There was, of course, no doubt that the circulation of the lesser involved extremity could be improved by operation, but that was not the patient's chief problem.

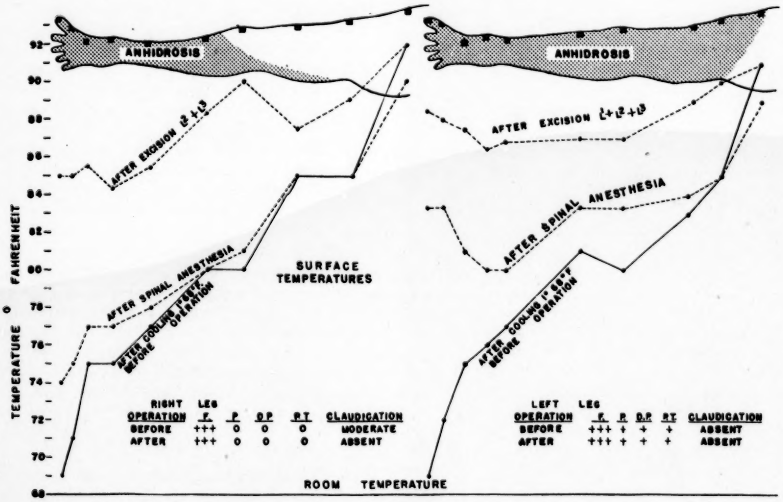

FIGURE 1.

Surface-temperature readings on both lower extremities of the same patient are compared after exposure to a room temperature of 68° F. for one hour. All four extremities were exposed, and the trunk was covered only by a sheet and thin cotton blanket from the axillas to the groin, to promote vasoconstriction. The patient was in the horizontal position. The degree of main-vessel obliteration differs in the two extremities. The effect of acute denervation following spinal anesthesia is compared with the change noted after surgical removal of certain lumbar sympathetic ganglia.

After operation, in response to cooling for one hour at 68°F., the surface temperatures remained much higher and were similar in the two extremities. It may therefore be stated that the circulation was significantly increased because vasoconstriction in response to prolonged cooling no longer took place. However, this does not mean that the circulation is greater in a warm environment after sympathectomy than it was before. In fact, the opposite is undoubtedly so. The one point that I should like to emphasize is that by interrupting vasoconstrictor pathways, one hopes to increase blood flow by stabilizing it somewhere near its maximal point. It should also be noted that in this case, intermittent claudication was relieved in spite of the continued absence of main-vessel pulsation. This indicates a favorable effect on the circulation to skeletal muscle, as well as the obvious increase to the skin and subcutaneous tissue. In addition, the characteristic distribution of anhidrosis involving the entire leg after excision of the first, second and third lumbar ganglia was indicated in the chart of the left leg after operation. On the right side, the removal of the second and third lumbar ganglia resulted in anhidrosis of the posterior thigh and the lower leg from the tibial tubercle distally. Figure 1 also emphasizes a clinical fact that has long been recognized: the effect of acute denervation of the blood supply to the extremities by procaine hydrochloride after exposure to and while in a cool environment does not, in the presence of the more advanced stages of obliterative vascular disease, indicate with accuracy what the effect of actual excision of appropriate portions of the autonomic nervous system will be.

This preliminary discussion of methods of study is given to present one viewpoint by which the effect of denervation of blood vessels on the

circulation of various organs and tissues of the body may be judged. I re-emphasize the fact that a quiet environment, absence of fear or worry or pain, the horizontal position and controlled room-temperature conditions are required for basal conditions of study.

Effect of Sympathectomy for Raynaud's Symptoms

Failure to observe these fundamental rules may be the cause for differences of opinion regarding the effectiveness of sympathectomy for various disorders, and may result in erroneous deductions and conclusions. This seems to me to be part of the explanation for the conclusions reached by Johnson[2] in a recent article in which he finds that sympathectomy is ineffective in the treatment of patients with Raynaud's symptoms. Other reasons for the poor results that he reports will be discussed subsequently. His conclusions are based on operations performed on thirteen upper extremities and two lower extremities of 6 patients. The studies on which his conclusions are drawn are the comparison of finger volume as measured by a plethysmograph before and after operation, and at times in response to local heat, and at times in response to novocaine block of the median nerves. The conditions under which the experiments were carried out are not described. No mention is made of the position of the patient, the manner in which the body was covered or the time allowed for adjustment to whatever environment was chosen before the tests were made. The room temperature is given in three of sixteen figures and varied from 23.5 to 27.3°C., or 74.3 to 81.1°F. This clearly indicates that the conditions for study were variable and not the sort to activate peripheral vasoconstriction.

From an analysis of the figures illustrating the article in question, it is clear that the surface temperatures of the digits were high in the studies carried out before operation. They varied from 24.6 to 34.2°C., or 76.3 to 93.6°F. After operation, they tended to be slightly higher. It is therefore obvious that these patients were not studied under conditions in which the autonomic nervous system was more than partially active. Particularly I refer to Figure 14 in Johnson's[2] article, in which finger-volume measurements were made when the digital surface temperature was 34.2°C. (93.6°F.) before operation for comparison with the state of affairs after operation. Under such circumstances, vasoconstriction is impossible and does not exist, and sympathectomy could not and does not result in an increase in surface temperature or blood flow. The point is not that sympathectomy does not increase peripheral circulation above its maximal preoperative level. The question is, Does sympathectomy prevent or modify a mechanism for reducing blood flow under the many conditions under which vasoconstriction exists? The answer is, In properly selected cases, the denervated extremity has a greater circulation under conditions when vasoconstriction ordinarily exists than the normally innervated extremity. This holds for normal extremities, for so-called "vasospastic disorders" and also, not infrequently, when organic vascular disease is the critical factor, such as arteriosclerosis, arteriolar disease and thromboangiitis obliterans. As organic vascular disease progresses, the maximal level of blood flow in the relaxed state decreases. The abnormal vessels, however, may still maintain their ability to constrict in response to nervous stimuli in a striking fashion. Under such circumstances, the need for modifying this latter mechanism assumes increasing urgency.

As further evidence of the ineffectiveness of sympathectomy, Johnson presents data showing that the vascular responses of an extremity to locally applied heat are not materially altered by sympathectomy. That increased blood flow to the extremity in response to local heat is controlled by local metabolic demands and not by the nervous system was shown by Freeman[3,4] years ago.

Surgical Technic, with Particular Reference to Denervation of Upper Extremity

It has long been recognized by many that the clinical results of postganglionic sympathectomy are not satisfactory because attacks of vasospasm recur after a few weeks, even in the absence of obvious local vascular disease, but particularly if such disease is present. Such attacks will occur in response to cold and also in a warm environment in response to emotion, such as might result from the demonstration of a patient before a group of physicians or students. The cold factor is eliminated under such circumstances. I have believed, and most observers have agreed, that this was probably the result of the action of circulating vasoconstrictor substances, and adrenin and sympathin appear to be likely ones.[5-7] After the preganglionic type of sympathectomy, the clinical results are far superior; such episodes as those described above in response to emotion do not occur, and vasospasm in response to cold appears only in the presence of significant degrees of local vascular disease. The attacks are milder, however, the recovery time is shorter, and the degree of exposure necessary to precipitate an attack is greater.

It is not surprising, therefore, on further perusal of Johnson's[2] article concerning the ineffectiveness of sympathectomy for Raynaud's symptoms, to find evidence of local fault of consequence in

some of the cases, but more particularly to find that the majority of the operations were of the postganglionic variety, which I discarded about ten years ago. In 2 cases, a preganglionic type of operation described by me[8, 9] in 1936 and modified several times since was used. That the denervation was not complete in 1 of these cases seems possible from the response to postoperative peripheral-nerve block, although as mentioned above, the surface-temperature level before nerve block was so high (91°F.) as to make it impossible to draw any accurate deductions. Evidence of the presence of intact vasomotor fibers in 2 of the 3 cases in which postganglionic operations were performed is also present in Johnson's data. He prefers to ignore this, and to endow somatic nerves with a vasomotor function, to explain postoperative responses that are the result of either incomplete interruption or regeneration of the vasomotor fibers. His attempt to explain a fall in temperature in the fifth finger after median-nerve block on the basis of shunting of blood from this finger to those supplied by the median nerve is far less convincing than the suggestion that this response is due to reflex vasoconstriction in the unblocked fifth finger as a result of the discomfort or excitement attendant on the nerve block. A transient fall in temperature of the first three fingers is commonly noted during ulnar-nerve block, and of all five fingers and more proximal portions of the hand, forearm and arm following paravertebral novocain block. Later, all denervated fingers reach the same high surface temperature unless the degree of local fault is more marked in some.

Atlas[10] has discussed the role of the second thoracic segment in the innervation of the upper extremity on the basis of a case in which this segment was not decentralized when a preganglionic type of sympathectomy was performed. He suggests that removal of the second thoracic ganglion alone is necessary to denervate the upper extremity. In this contention, he is correct. From personal observation of a number of cases in which the second thoracic ganglion was not excluded for one reason or another, it is clear that in the majority of patients, but not all, the second thoracic segment supplies fibers of consequence to the brachial plexus. However, division of the trunk above the second dorsal ganglion, with or without excision of this ganglion, excision of the second and third dorsal ganglia, and excision of the first and second dorsal ganglia have all been followed, in my experience, by significant regeneration. I have no reason to believe that simple excision of the second dorsal ganglion, which Atlas suggests as a method of denervating the upper extremity, will prevent regeneration. This major problem was recently discussed in detail.[11]

Physiology — Blood Flow, with Particular Reference to Hypertension

In a series of four articles, Wilkins and Eichna[12-15] have studied blood flow to the forearm and calf in great detail. The conditions for study were well standardized in all observations. Measurements of blood flow were made by means of a segment plethysmograph. The primary purpose of the study was to gather information concerning the peripheral circulation in cases of essential hypertension. In particular, the authors wished to determine whether the increased peripheral resistance to blood flow is due to an irreversible type of change in the walls of the arteries. Furthermore, they wished to gather more information concerning the role of the sympathetic nervous system in regulating the peripheral resistance to blood flow in both normal and hypertensive patients. In these studies, blood flow was determined in normal subjects, in patients with vasomotor disorders and in hypertensive patients. The response to various stimuli designed to activate the autonomic nervous system was observed. The effect of inactivation of the nervous system by nonoperative and operative intervention was determined. The findings are presented in detail and in such fashion that those interested in this matter will find a large number of valuable data.

These authors observe that in the forearm and calf, reflex vasodilation on warming and reflex vasoconstriction on cooling of the body are mediated by the sympathetic nervous system. It is therefore apparent that the changes in circulation in the more muscular portions of the extremities are qualitatively similar to those in the hands and feet, although they are quantitatively not so great. These reflex changes in the more muscular areas are abolished by preganglionic sympathectomy, and blood flow is stabilized at a point somewhere between the high and low levels observed in the undenervated state. As pointed out above, the blood flow in the deeper tissues is likewise reduced after preganglionic sympathectomy when compared to the maximal and increased when compared to the minimal blood-flow levels observed in the undenervated state.

It is of interest that blood flow to the muscular areas of the extremities increased after sympathectomy in response to exercise exactly as it did in the undenervated state. This increase was also observed following reactive hyperemia induced by a five-minute period of circulatory arrest. Moreover, blood flow to these areas increased in response to local heat after sympathectomy as before, although at the temperature level selected (40°C.) the increase after operation was not quite so marked. It is therefore quite clear that certain

major physiologic responses are preserved in the denervated state, and that the necessary stimulus for their initiation is derived primarily from the tissues. A delayed vasodilator response generally induced by mental arithmetic was noted both before and after sympathectomy. This was similar to that resulting from the administration of a small amount of epinephrin. In 2 hypertensive patients, this response disappeared after adrenal denervation resulting from bilateral splanchnic and lumbar sympathectomy; it is interesting that it disappeared both in the denervated calves and in the undenervated, normally innervated arms. Muscular blood flow, which was also studied in the presence of disturbed thyroid activity, was found to vary in the same direction as the metabolic rate.

Reactive hyperemia blood flow was measured in normal and hypertensive patients. A direct relation between arterial pressure and blood flow was found in both denervated and undenervated extremities of normotensive and hypertensive patients. When the same conditions of vasodilation were imposed, there was no significant difference between the blood flow to the forearm and calf in certain normal subjects in whom rises in arterial pressure had been induced and that in certain hypertensive patients; nor was there any difference between the blood flow to the forearm and calf in certain hypertensive patients whose arterial pressures had been lowered and that in normal subjects with the same arterial pressure.

Wilkins and Eichna find their data consistent with the view that in certain hypertensive patients the blood flow to the forearm and calf during controlled vasodilation is greater than the normal for those subjects. Their study has raised doubts in their minds concerning the validity of previous conclusions that in patients with essential hypertension the vessels of the muscular segments of the limbs are involved in a generalized increased peripheral resistance that cannot be released by physiologic vasodilatation.

A series of very valuable articles and monographs has been written by Smith and his coworkers[16–21] in recent years concerning renal blood flow in hypertensive patients. They have devised an accurate method for measuring the quantity of blood flowing through the kidneys per minute by means of inulin and Diodrast clearances. They have demonstrated clearly that the autonomic nervous system, when activated either by pain or by emotion in the horizontal position, reduces blood flow through the kidneys by constricting the afferent arterial supply. They have also shown that renal blood flow is reduced by nervous control when the patient shifts from the horizontal to the upright position; this is likewise due to constriction of the afferent arterioles. They also find that adrenin is capable of reducing renal blood flow but acts principally on the efferent arterioles. They observed that renal blood flow was maximal in the horizontal position, and was not increased by acute denervation of the renal blood supply resulting from spinal anesthesia. It seems reasonable, therefore, to hope that if the sympathetic nerve supply to the kidneys and adrenal glands is thoroughly interrupted by a surgical procedure, renal blood flow will be more stable and increased by comparison with the low levels resulting from vasoconstriction due to intermittent nerve impulses and reflex adrenal secretion. One would not expect it to be increased by comparison with maximal blood-flow levels in the undenervated state. Since the renal blood-flow level is almost always reduced in the hypertensive state by comparison with the normal, it is essential to stabilize and if possible to preserve what remains.

Clinical Results, with Particular Reference to Surgical Treatment of Hypertension

Further reports of the clinical results of surgical intervention on the autonomic nervous system for essential and malignant hypertension have appeared in the literature. The operations devised vary considerably in extent. Also, the percentage distribution of cases in the different stages of the disease, as judged by eyeground changes, varies a great deal in the reported series. For example, Allen and Adson[22] employ an operation in which the nerve supply to the splanchnic bed is interrupted as completely as possible by an exposure that is entirely below the diaphragm. In a series of 224 patients, grouped according to eyeground changes, 5 per cent of the cases were in Group 1, 61 per cent in Group 2, 31 per cent in Group 3, and 3 per cent in Group 4. They found a significant reduction of blood pressure in 45 per cent of cases in Group 1, 35 per cent in Group 2, 26 per cent in Group 3, and 0 per cent in Group 4. For the groups as a whole, 31 per cent of the patients had a significant lowering of blood pressure.

Peet, Woods and Braden[23] report their experience with the supradiaphragmatic technic in which the operation is confined to the region immediately above the diaphragm. Its purpose is similar — to denervate the splanchnic bed as completely as possible by interrupting the portion of its nerve supply that is accessible at this level. The authors believed that the majority of their patients (70.7 per cent of 290 patients followed nine months to seven years) had a significant

lowering of blood pressure. Of these 290 cases, it appears that more significant evidence of lowering of blood pressure occurred in 19.3 per cent. These cases were not classified into groups according to eyeground changes. It is therefore impossible to discern the relative effect on blood pressure in the various stages of the disease. The eyeground changes were given in a series of 219 cases. In 10, the eyegrounds were normal, 13 were in Group 1, 50 in Group 2, 105 in Group 3, and 42 in Group 4. One may infer from this that the majority of the patients were in the more advanced stages of the disease.

More recently, Woods and Peet[24] have compared the mortality rate in 76 cases followed from five to seven years after operation with that described by Wagener and Keith[25] for medically treated patients. The effect on blood-pressure levels for 60 cases followed nine months or more is given. Of 4 cases in Group 1, the blood pressure was reduced in 1 (25 per cent), and of 9 cases in Group 2, a reduction occurred in 2 cases (22 per cent). Blood-pressure reduction was noted in 15 (48 per cent) of 31 cases in Group 3, and in 7 (44 per cent) of 16 cases in Group 4. The latter figures are encouraging, but the results in the cases in Groups 1 and 2 are not. Woods and Peet found the survival period in cases in Groups 1, 3 and 4 to be higher than that reported by Wagener and Keith. They noted, however, that in Group 2, the survival period was higher in the medically treated cases. The explanation for these findings is not clear. It is suggested that the significant fact was that patients in Group 2 were those with well-defined arteriolar sclerosis, without angiospasm of the retinal vessels. It is doubtful if an accurate prediction of the operative result can be made primarily on eyeground changes in the various stages of essential hypertension. Experienced ophthalmologists vary widely in their descriptions of vascular alterations in the fundi. A classification that takes into account the state of the brain, eyes, heart and kidney should be more helpful. One change about which there is no difference of opinion is the presence of papilledema. Since this constitutes the sole criterion for the diagnosis of malignant hypertension, the survival rates in Group 4 cases is significant: 33 per cent at the end of five years in the operated group, and 2 per cent in the medically treated group.

Experiences with supradiaphragmatic, subdiaphragmatic and combined lumbodorsal splanchnicectomy[26] were discussed by de Takats et al.,[27] who found the latter operation to result in a more significant lowering of blood pressure. Heuer and Glenn[28] report the late results of experiences with the surgical treatment of hypertension in 57 patients. Three operations were used — laminectomy, with anterior-root section, and supradiaphragmatic and subdiaphragmatic splanchnicectomy. In the opinion of the authors, the results justify a continuation of surgical attempts to relieve hypertension, but the operation should be extensive. They favor combined lumbodorsal splanchnicectomy because it is more complete than laminectomy and anterior-root section, which had to be abandoned because of the high mortality and incidence of serious complications. However, the best results, when judged by persistent lowering of blood pressure, appeared to follow this operation.

Corcoran and Page[29] report the effect of lumbodorsal splanchnicectomy on renal blood flow in 2 cases. There was no immediate increase; in fact, there was a decrease in both. The authors considered the effect on blood pressure to be significant, however, and suggested that in time this might result in a regression of vascular disease generally and in the kidney as well, and might, in this way, exert a favorable effect on the renal humoral mechanism.

Lumbodorsal splanchnicectomy,[26] which was devised more than three years ago, has been used during this period. It appears to have the advantages of both the supradiaphragmatic and subdiaphragmatic procedures, and is a little more extensive than both combined. The early results have been reported in a preliminary fashion[1,30] and will be given in detail this year. The operation affords excellent exposure of the kidneys and adrenal glands. Considerable information concerning the actual state of the renal blood vessels in various stages of the disease has been obtained from a study of renal biopsies. A preliminary report of these findings was made by Castleman et al.[31] In some cases, quantitative studies of renal blood flow have been made by Talbott.[32] It is hoped that these data when correlated with other detailed studies will help in the selection of cases for surgery.

Early experiences with total and nearly total sympathectomy performed in closely approximated stages in a small series of hypertensive patients were reported by Grimson.[33] The rationale was based on experiences with experimental hypertension in dogs. It seemed to me[34] that the indications for extending the surgical approach to hypertension in man beyond the splanchnic area should depend on a careful evaluation of the results of the latter maneuver and not on the results of experimental surgery. Although certain patients may benefit by greater than radical splanchnicectomy, it is doubtful if such an operation should, at present, become a routine primary procedure.

It seems quite clear that surgery has something worth while to offer the hypertensive patient. It appears that, if consistent results are to be obtained in similar cases, radical denervation of the splanchnic bed is necessary. It is also obvious that when cardiac and renal functions are both significantly impaired, operation is of no avail, however extensive. Only an occasional patient over fifty years of age is suitable for operation. When the indications for operation are clearly defined, it is to be expected that a high percentage of carefully selected patients will benefit, as judged by persistent and significant lowering of blood-pressure levels. Regression of eyeground changes, decrease in the size of the heart, improvement in the electrocardiogram, improvement of renal function and at times, of renal blood, and relief of symptoms are noted in certain cases and present additional ways of evaluating the results of surgery. Furthermore, time may show that life expectancy is increased. There can even now be no doubt of such an increase in cases of malignant hypertension and in patients with severe retinitis who have been subjected to adequate surgery before cardiac and renal functions have been seriously impaired. At the present time, surgery appears to offer the greatest hope for these patients. Perhaps, some day, a simpler solution will be attained.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28151

PRESENTATION OF CASE

A sixty-eight-year-old physician was admitted to the hospital because of an acute illness.

Five nights before entry, the patient suddenly lost consciousness. On regaining consciousness, after about three hours, he complained of very severe frontal headache, and vomited twelve to fifteen times within the next hour and a half. In this period he felt drowsy and dizzy. Subsequently, he was kept in bed under sedation. There was occasional vomiting. Most of the time, the patient had severe headache. There were never any paralyses, pains or respiratory difficulties.

Seventeen years earlier, the patient had an appendectomy performed in the hospital, and a year later the gall bladder was removed because of chronic cholecystitis. About two and a half years before entry, he had attacks diagnosed as "coronary thrombosis" by a physician.

On admission, the patient appeared drowsy, but co-operative and well oriented, complaining of severe frontal and temporal headache. The face was plethoric, and the pupils reacted hardly at all to light. The right fundus showed blurring of the disk and distention of the veins. The neck was moderately stiff. There was a Babinski plantar response on the right, and a questionable Babinski response on the left. There were no other abnormal reflexes, and no muscular weaknesses or sensory changes. The heart was enlarged to the left, and a harsh, rough, apical systolic murmur was audible all over the precordium.

The temperature was 98.6°F., the pulse 50, and the respirations 10. The blood pressure was 140 systolic, 65 diastolic.

The Hinton blood reaction was negative. The urine showed a + test for albumin, with occasional red and white and epithelial cells in the sediment.

An electrocardiogram showed sinoauricular tachycardia (rate 145 to 150), slurred QRS complexes, diphasic T_1 and T_2 waves, moderate left-axis deviation and a rare ventricular premature beat.

On the second hospital day, after returning to bed from the toilet, the patient suddenly cried out because of pain in his head, and lost consciousness. There were no convulsive movements, or marked changes in color. About ten minutes later, Cheyne–Stokes respirations appeared. The patient's face turned gray, and the lips flaming red. The neck was somewhat resistant to bending forward. The right eye turned outward, and the left was fixed centrally. The heart was regular, except for slight variation with respirations (pulse 60 to 70). There was no change in the heart murmur. The lungs were clear. Suddenly, the patient became very flushed, with gasping respirations and coarse tracheal rales. The patient soon stopped breathing, cyanosis deepened, and the heart beats ceased.

DIFFERENTIAL DIAGNOSIS

DR. MAURICE FREMONT-SMITH: There are three hurdles in this case that I may not be able to clear. In the first place, we do not have any past history, except some noncontributory data such as appendectomy and cholecystectomy, which had nothing to do with the present situation. We do know that the patient was sixty-eight years of age, was said to have had a coronary thrombosis and was, according to the history, running along well until he had this sudden difficulty.

The second hurdle is that we have no record of a lumbar puncture and examination of the spinal fluid. I assume that if a case has had a spinal-fluid examination it is a neurologic case and a neurologist discusses it; if it does not, it is a medical case and a medical man discusses it.

The third hurdle, the chief one, is the limitation of a medical man in the discussion of things neurologic.

Five days before he came in, the patient had a sudden acute episode that could be interpreted only as an intracranial accident, with the rapid development of increased intracranial pressure. He became unconscious and vomited frequently. He had severe headache. The onset was extremely sudden and, in a man of sixty-eight, suggests some sort of vascular accident; the stiffness of the neck makes one believe that subarachnoid hemorrhage was the likeliest diagnosis. On the other hand, it is unusual to have subarachnoid hemorrhage at this age. It is usually the result of congenital anomaly, and usually occurs earlier than this. Moreover, with a subarachnoid hemorrhage as with any type of meningeal irritation, fever is the rule, and this man had no fever. I remember, in discussing a case a few weeks ago, Dr. Kubik brought up the fact that, with subarachnoid hemorrhage, very frequently albumin and red cells of unknown origin appear in the urine, so that we can accept the albumin in our hypothetical diagnosis of subarachnoid hemorrhage. On the other hand, further possibilities must be considered. Was

this man well, or was he having some symptoms before the onset of this acute episode? He could have had a brain tumor, and this sudden episode could have been hemorrhage into the tumor. If so, we must assume that the hemorrhage had extended into the subarachnoid space, because he had meningeal irritation. He could have had meningitis, but a meningitis is usually much slower in onset and there should be some fever. Unconsciousness would come late. Lumbar puncture would be almost essential in making this diagnosis.

The patient could have had some sort of injury. He might have fractured his skull previously; we have no history. He might have had a subdural hematoma. There again, the blood must have gone into the subarachnoid space. He might have had a subacute bacterial endocarditis with embolism to his brain. He was very old for that, but he had a rough systolic murmur. I should like some comment from the neurologist afterward. I believe it would be very unlikely to have meningeal signs from such a lesion. We have the interesting fact that the patient had no paralysis. He had a Babinski response on the right, and a questionable one on the left. So that if we try to localize it, we should assume the greater injury or difficulty on the left side of the cerebrum. On the other hand, when the choked disk was described, it was the right fundus that showed blurring, and I am unable to interpret the development of this unilateral choked disk. I believe that it must be very important. It is a very rapid development: within five days, the patient had a markedly choked disk on one side. I do not know how to explain that.

Regarding embolism from the heart, if the patient had had an old coronary thrombosis he might have had a thrombus in the left side of the heart,—a mural thrombus,—and he might have thrown that off into the brain. On the other hand, the electrocardiogram does not suggest coronary thrombosis. I should interpret the electrocardiogram as showing arteriosclerotic coronary heart disease, but without evidence of thrombosis.

It is interesting that he was allowed out of bed in the hospital after this accident. Either it was against orders or they did not think he was seriously ill. He got out of bed, walked to the toilet, had a recurrence of whatever happened to him originally, and died with increasing signs of intracranial pressure and some localized paralysis of the right eye or both eyes. I am going to ask subsequently if the neurologist will make a comment about this. I cannot understand the lesion behind that type of paralysis.

Accordingly, because he was sixty-eight years old, I believe the patient had a vascular accident of some type, perhaps a subarachnoid hemorrhage. He had a low blood pressure. Did he always have it? Was the blood pressure usually high, and did it come down either because of cardiac insufficiency or because of the shock occasioned by his recent lesion? If he had had increasing or increased intracranial pressure, the blood pressure should have risen. The blood pressure, however, was not high, but the pulse was slow; he had choked disks, and he had, I think, increased intracranial pressure. I should like to leave the case open for discussion from the floor and ask the neurologic experts to add something.

My diagnosis is intracranial vascular accident, probably subarachnoid hemorrhage. If the patient had had an intraventricular hemorrhage, I think he would have been sicker, have had convulsions, and not have regained consciousness; and I think it is more likely a straight subarachnoid hemorrhage. Without hypertension, I suppose that, even at this age, the basis for hemorrhage was a congenital aneurysm.

DR. WILLIAM B. BREED: I am not a neurologist, but I should like to ask a question. Do you think perhaps the meningeal, subarachnoid phase of this has been overemphasized? The only evidence is some stiffness of the neck, only slightly painful.

DR. FREMONT-SMITH: It is quite important evidence. One sees a patient with almost no neurologic signs, perhaps a headache, but if only slight stiffness of the neck is present one may suspect a diagnosis of encephalitis as against a simple upper respiratory infection. I think that this sign is important if present. One thing to remember is that in stiffness from meningeal irritation the neck resists forward bending, but the head can be easily turned from side to side. In arthritis, on the other hand, all motions of the head are painful. I prefer to believe that the symptom is important in this case.

A PHYSICIAN: Does it not say later that it became stiff?

DR. FREMONT-SMITH: The last note says, "The neck was somewhat resistant to bending forward." I should accept that as an important sign.

DR. TRACY B. MALLORY: Does anyone care to comment on Dr. Fremont-Smith's question regarding meningeal irritation secondary to emboli from a bacterial endocarditis?

DR. CHARLES S. KUBIK: We have had a fair number of cases in which cells, although usually no organisms, were present in the spinal fluid and a subarachnoid exudate was found on post-mortem examination. The condition presumably results

from emboli to meningeal vessels. Another possibility is bleeding from a mycotic aneurysm.

In answer to Dr. Breed's question, another point in the history must be considered: all this patient had was a stiff neck and headache, but the symptoms came on suddenly, and at the onset he lost consciousness.

Dr. James B. Ayer: I saw this patient at home on the third day of his illness. He was mentally clear, admitting slight headache. Except for slight stiffness of the neck, neurologic examination was negative. The heart was as described. I believed that we were dealing with cerebral embolus and asked Dr. Paul White, who had followed him, if the heart was consistent with this diagnosis. He agreed. I saw the patient the next day. The neck was still very slightly stiff, and there was still headache. Kernig's sign was absent, and the fundi were normal. Although the diagnosis of cerebral embolus still seemed to me correct, it was decided to send the patient to the hospital for further study. A lumbar puncture was planned for the morning of his death. Had it been done before death, I should certainly have considered it a contributing factor. As it was, his unexpected walk to the toilet room seems to have been the predisposing act. The second episode naturally weakened my opinion about the diagnosis of embolus. Yet we had no evidence for tumor or any long-standing disease other than that of the heart. I was reticent about making a diagnosis of spontaneous subarachnoid hemorrhage, and still favored the diagnosis of embolus.

A Physician: I wonder if you would say a word about the ocular paresis.

Dr. Ayer: Yes; there was a slight paresis, which certainly was a little in favor of Dr. Fremont-Smith's diagnosis.

Dr. Jacob Lerman: Did Dr. Fremont-Smith commit himself about the heart?

Dr. Fremont-Smith: I did say that I thought the electrocardiogram gave no evidence of past coronary thrombosis.

Clinical Diagnoses

Cerebral hemorrhage?
Cerebral embolus?
Old myocardial infarction.

Dr. Fremont-Smith's Diagnosis

Subarachnoid hemorrhage from congenital aneurysm.

Anatomical Diagnoses

Congenital aneurysm of right internal carotid artery and circle of Willis, with rupture and hemorrhage into subdural and subarachnoid space.
Cardiac hypertrophy, hypertensive type.
Infarct of heart, healed.
Arteriosclerosis, marked, generalized.
Nephrosclerosis, moderate.
Operative scars: cholecystectomy and appendectomy.

Pathological Discussion

Dr. Mallory: The heart was hypertrophied and showed marked diffuse coronary sclerosis. All the vessels were narrowed down to pinpoint lumens, but there were no points of complete occlusion. The left ventricle showed considerable patchy fibrous scarring of the inner third of the myocardium, consistent with old infarction, two or three years old perhaps. There was no overlying thrombus, however, and no thrombi in any of the other cavities, and there were no valvular deformities or anything to explain the heart murmur.

Dr. Kubik will describe the cerebral findings.

Dr. Fremont-Smith: May I ask Dr. Bland if it is usual for an old coronary thrombosis to give a later electrocardiogram like this?

Dr. Edward F. Bland: It may be anything from normal to the findings recorded here.

Dr. Mallory, would you be willing to comment on emboli following coronary thrombosis? It often comes up in these discussions.

Dr. Mallory: It is my impression that, if an embolus occurs following infarction, it follows after a relatively brief period; in the first month, it is not unusual, but subsequent to that it is quite uncommon.

It is generally true that emboli from a mural thrombus overlying an infarct are apt to be large massive ones, not the type that might plug a small vessel in the brain. It is more apt to be an enormous embolus that goes down the aorta and forms a rider at the bifurcation of the iliac arteries or plugs the whole femoral artery on one side.

Dr. Kubik: There was a ruptured aneurysm in the outer angle between the right internal carotid and posterior communicating arteries. Although these are called congenital aneurysms, it is quite possible that they may not always date from birth. They always occur in the fork between a larger artery and one of its branches, or between two branches of the same size. It is not uncommon to find a defect in the media at this point. It is the defect that is congenital, and an aneurysm is probably an enlarged defect, which, in some cases, is present at birth but may develop, in other cases, after birth on the basis of the congenital defect. There is no media in the wall of the aneurysm, only intima and adventitia. Most of those observed in this laboratory have involved the internal

carotid, middle cerebral or anterior cerebral artery. There have, I believe, been only two of the basilar artery.

DR. MALLORY: I think is is fair to say that as we have become increasingly conscious of the relation of aneurysms of this type to cerebral accident, and particularly to subarachnoid hemorrhage, we are finding them with considerably increased frequency even in people beyond fifty, as in this case.

A PHYSICIAN: May I ask about the kidneys?

DR. MALLORY: They showed very slight contraction consistent with a slight degree of hypertension. The patient may very possibly have had hypertension before his cardiac infarct. I do not know specifically.

DR. HENRY R. VIETS: Was there much blood in the subarachnoid space, or little?

DR. KUBIK: There was a good deal.

DR. VIETS: It is interesting that he did not have convulsions.

DR. KUBIK: The hemorrhage had not extended into the substance of the brain, as it sometimes does.

DR. VIETS: We can say, then, that the stiff neck was important.

DR. ALLEN G. BRAILEY: Was not the low blood pressure an unusual finding?

DR. MALLORY: The patient may well have had a hypertension that disappeared with the cardiac infarct. That is not an uncommon story.

CASE 28152

PRESENTATION OF CASE

A twenty-seven-year-old housewife was admitted from an outside hospital, because of coma, following stiffness of the neck.

A week before entry, the patient awoke one morning with a stiff neck. There were no other complaints. A physician found the neck to be fairly rigid, with some voluntary spasm of the right trapezius muscle. The neck could be moved laterally without much difficulty, and could be flexed passively. The blood pressure was 145 systolic, 90 diastolic, seated. The temperature, pulse and respirations were normal.

There was no history of antecedent trauma. Ten years previously, the patient had been operated on for a benign ovarian cyst.

The neck was treated with local heat and rest. In the next three days, there was much improvement, so that the patient went to a dance, feeling well. The next afternoon, the stiffness in the neck returned, and local heat failed to help. Two days before entry, the patient again consulted her physician. Examination showed inability to flex the head because of pain and stiffness on the right side of the neck, extending upward to the right occipital region. Lateral motion was restricted on the left, but fairly free on the right. The reflexes were normal, with a negative Kernig's sign. The pupillary reactions and the fundi were normal. The temperature, pulse and respirations were normal. Bed rest, aspirin and local heat were advised. On the morning of entry, the patient complained of headache centering in the right parieto-occipital area. A cough made her feel "as if the top of the head were coming off." The pupils were small, and reacted poorly to light. She was admitted to an outside hospital, with a temperature of 98.8°F., a pulse of 68 and respirations of 20; the blood pressure was 150 systolic, 90 diastolic. Examination of the blood showed a white-cell count of 12,000. The urine was normal. The patient was put to bed, and given sedation. She dozed for an hour, then awakened suddenly and cried out in pain. The right arm and leg twitched. She was unable to speak, but seemed oriented. The pulse was 60, the respirations were shallow, and there was slight cyanosis. Oxygen and intramuscular magnesium sulfate and caffeine were given. In about three minutes, there was gradual recovery. The blood pressure was then found to be 210 systolic, 110 diastolic. The patient was fully conscious, rational and able to talk. She said that her headache had abated. She remained quiet for about two hours, when there was a second attack similar to the first. The right arm and leg twitched, and then became fixed in rigid extension, with the right foot in Babinski position. After twenty minutes, the left arm and leg progressed through a similar phase of twitching to a similar type of spasticity. The rigidity of the neck had disappeared. There were no facial twitchings. The pupils were constricted. There was continued unconsciousness. The systolic blood pressure varied between 160 and 180. The respirations were shallow, varying from 20 to 30, and even in an oxygen tent the color was dusky. The pulse remained at 60. The patient was transferred to this hospital by ambulance.

On admission, the patient was apneic, with a pulse between 130 and 150. There was some question of early edema of the medial sides of both optic disks. The patient was maintained in a respirator for about an hour, when the heart stopped.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES S. KUBIK: A young woman was admitted in coma, following stiffness of the neck of a week's duration. There was no paralysis.

If, as one may assume, the patient had been in good health, there are not many diseases that would result in such a sequence of events. One might think of meningitis and spontaneous subarachnoid hemorrhage, but meningitis ought to be ruled out by the absence of fever and by a temporary remission of symptoms. There is still another reason for ruling out meningitis. This patient did not have any headache until several days after the onset of her illness. The absence of headache, to be sure, very nearly rules out subarachnoid hemorrhage. Headache is usually the first and one of the most prominent symptoms, but there are occasional cases without headache. I have heard of two, and there is a patient in the hospital now whose headache, which was severe at the onset, quickly subsided although the neck was rigid and movements of the neck were painful, the pressure was very high, and there were signs of active bleeding in the form of convulsive seizures and increasing hemiparesis.

But, returning to the case under discussion, one week or so after the onset of stiffness of the neck the patient did complain of headache, centering in the right parieto-occipital region, and when she coughed it felt as if the top of her head were coming off. These symptoms were more typical of hemorrhage and increasing intracranial pressure. Then, shortly after being admitted to the outside hospital, she cried out with pain, which, I assume, signified a sudden increase in the severity of the headache; however, it may have been due to pain in the neck, or both. In any event, the sudden onset and severity of this pain compel one to think of bleeding, and nothing else.

From this point on, the course was more or less characteristic of severe intracranial hemorrhage, and consistent with subarachnoid hemorrhage that had broken through the pia mater into the brain or ventricle, with a marked and rapid increase in intracranial pressure. Such a situation best explains the seizures, elevation of blood pressure, slowing of the pulse, shallow respirations and, finally, respiratory failure. Toward the end, the pulse became rapid, presumably because of paralysis of the vagal centers in the medulla.

Could this have been a cerebral or pontine hemorrhage? I should think not. The patient was young; she did not have hypertension or, at any rate, not marked hypertension, and there was no paralysis.

I recall a case of cerebellar hemorrhage, with rupture into the fourth ventricle, that ran a course similar to that of subarachnoid hemorrhage. In that case, I believe, there was considerable vertigo. I mention this because of the right-sided pain in the neck but have no right to offer it as a diagnosis. The possibility of cerebral or cerebellar tumor, other than vascular tumor and of abscess or subdural hematoma can, I should think, be dismissed without any further comment.

If this was a subarachnoid hemorrhage, what and where was the source of the bleeding? By far the most common cause, as you all know, is so-called "congenital aneurysm." Less common causes are varices, cavernous hemangioma, hemangioma of choroid plexus, mycotic aneurysm and hemorrhagic disease. I do not see any special reason for suspecting any of these less common conditions, and my diagnosis will therefore have to be ruptured congenital aneurysm. The violence of the terminal stage of the illness suggests arterial rather than venous bleeding.

The aneurysms, in my experience, are most often found on the internal carotid, middle cerebral or anterior cerebral arteries, occasionally on the basilar. In this case, possible leads to localization are somewhat bewildering. Rigidity of any pain in the neck, without headache, observed at the onset, might point to the posterior fossa. A small amount of bleeding there might conceivably cause considerable rigidity of the neck without increasing intracranial pressure very much. Small pupils, reacting poorly to light, also suggest a disturbance in that locality. It is a matter of experience that fixed pupils in subarachnoid hemorrhage are of no localizing value; but the pupils in this case also became constricted, and that might mean something. There were no other signs of cranial-nerve involvement to help one in making a localization.

What can one do with the seizures? These began on the wrong side,—that is, on the same side as the headache,—then involved the other side, and were followed by what was probably extensor rigidity. They might suggest aneurysm of the internal carotid, middle cerebral or anterior cerebral artery, possibly the anterior cerebral, which lies in the intercerebral fissure, so that the hemorrhage might have extended first into one and then into the other frontal lobe or, what is commoner, upward through the rostrum of the corpus callosum into the anterior horns of the lateral ventricles. But if that had been the site of the bleeding, one would have expected frontal headache and pain back of the eyes. I believe that I have seen seizures such as these, and extensor rigidity as a terminal event in subarachnoid hemorrhage even when there was not extensive hemorrhage into the substance of the brain. The ventricles may even be distended with blood entering through the cistern, fourth ventricle and aqueduct. Perhaps the seizures are not of localizing significance and can be explained by an aneurysm of the basilar artery rupturing into the third ventricle. I have

seen a mycotic aneurysm at the bifurcation of the basilar artery that did so. Rapid and marked elevation of intracranial pressure could be responsible or partly responsible for seizures. In a case of subarachnoid hemorrhage not long ago, seizures stopped almost immediately after the pressure was lowered by lumbar puncture. This happened three times. In any event, I believe that the right-sided pain and headache are of more localizing value than the initial right-sidedness of the seizures. With the exception of a certain percentage of internal carotid aneurysms, which, when they bleed, result in paralysis of the third nerve, localization of a bleeding aneurysm is usually difficult and uncertain, and I am not competent to make a localization in this case. If I had to make a guess, I should say an aneurysm of the basilar artery on the right side, but, since these are not common, the odds are not favorable.

I should expect to find blood in the ventricles and a cerebellar pressure cone.

DR. MAURICE FREMONT-SMITH: Both this patient and the preceding one, whose case I discussed, were followed for five days or more, and in neither case was fever noted. Am I wrong in believing that it is usual in subarachnoid hemorrhage to have a rise in temperature after forty-eight hours?

DR. KUBIK: Very frequently, although not in every case, the temperature is elevated.

DR. JAMES B. AYER: The white-cell count, too, is commonly increased.

DR. AUGUSTUS S. ROSE: From the physiologic standpoint, could not stiffness of the neck and the extensor rigidity be explained by neoplasm of the posterior fossa?

DR. KUBIK: Yes; in some cases of cerebellar tumor, the patients do complain of attacks of severe pain in the neck, which may come on rather suddenly, but I see no reason for suspecting a tumor in this case. The patient had no symptoms previously. She was, I assume, perfectly well. The whole course was too rapid for tumor.

DR. FREMONT-SMITH: Would she not have had cerebellar signs in that case?

DR. KUBIK: I should think so.

DR. CLEMENS BENDA: How do you explain the stiffness of the neck before she had the bleeding?

DR. KUBIK: I think that there must have been bleeding, although, at the beginning, not a large hemorrhage. Aneurysms, before they begin to leak, are practically always asymptomatic. I doubt whether a large rupture or "blow-out" of the aneurysm is ever followed by recovery or remission of symptoms.

CLINICAL DIAGNOSIS

Brain tumor?

DR. KUBIK'S DIAGNOSES

Ruptured congenital aneurysm.
Subarachnoid hemorrhage.
Cerebellar pressure cone.

ANATOMICAL DIAGNOSIS

Congenital aneurysm in outer angle between the right internal carotid and posterior communicating arteries.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: At post-mortem examination, very extensive subarachnoid hemorrhage was found, and all the ventricles were filled and distended with blood. There was destruction of the floor of the third ventricle, but no other point of destruction of the cerebral substance. At the time of autopsy, no aneurysm could be identified, but later, after fixation and careful dissection, a very small aneurysm was found in the outer angle between the right internal carotid and posterior communicating arteries. There was a cerebellar pressure cone.

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MEDICAL-SERVICE PLANS

The recent Conference on Medical-Service Plans, held in Chicago under the auspices of the American Medical Association, gives evidence of the nation-wide interest in this movement. Sixty-four persons attended, including representatives from operating and proposed medical-service plans in seventeen states. As Dr. Olin West stated in his opening address, the conference was called to exchange information and opinions and thus to obtain an understanding of the basic problems.

The development of prepayment medical-service plans has chiefly involved three types of organization: the group clinic or consumer group, of which there are seventeen in operation, with a total enrollment of 100,000 persons; the employee-employer mutual-benefit association, of which there are about three hundred, and the commercial insurance company, with about two hundred and fifty plans, all of which provide cash indemnity benefits of $365,000,000 annually; and the nonprofit medical-service plans sponsored by medical societies, of which thirty-three are operating in nine states, with an enrollment of about 750,000 persons. Within the last few years, the last type has developed rapidly and appears to offer the best means for a proper distribution of medical service.

Some of the particularly pertinent points brought out in the discussion were as follows: satisfactory medical service for an entire community can be provided only by an all-inclusive plan, rather than one limited to a few physicians; the threat of compulsory sickness insurance is abetted by a multiplicity of lay-controlled or commercial plans but thwarted by medically sponsored community programs; an investigation should be undertaken to determine the effect of complete-coverage plans on the private practice of medicine; to be eligible for increased fees, a specialist must strictly confine his practice to his specialty; group enrollment furnishes a better group of subscribers than one based on individual physical examinations; a somewhat uniform model of legislation for medical-service plans should be adopted; a committee should be created to confer with one representing the hospital-service plans, to determine how and to what extent joint operations are possible; and a centralized agency should be established for the collection and dissemination of information.

At the conclusion of the conference, a committee of five was appointed to determine the best method of establishing a permanent organization of the medical-service plans throughout the country. This committee will meet with the Board of Trustees of the American Medical Association and will act in conjunction with the Bureau of Medical Economics of the American Medical Association. Dr. James C. McCann, chairman of the Committee of Prepayment Medical-Care Costs Insurance of the Massachusetts Medical Society, is a member of the national committee—a fact

that takes cognizance of the adroit and intelligent manner in which he has handled the promotion of the Society's medical-service plan in Massachusetts.

NATIONAL FOUNDATION FOR INFANTILE PARALYSIS

THE National Foundation for Infantile Paralysis has completed three years of work since its organization. This new and active group, covering the entire field of investigation into the cause, prevention and amelioration of poliomyelitis, is supported by a fund-raising agency, the Committee for the Celebration of the President's Birthday. Through various medical committees, activities are carried out in virus and nutritional research, the prevention of aftereffects, the study of epidemics and the dissemination of educational information.

In 1941, according to the annual report,* the largest grants for research went to the virus-research committee. A sum of over $185,000 enabled investigators in many states to pursue their studies. Large grants were made to the School of Public Health of the University of Michigan, the George Williams Hooper Foundation of the University of California, Yale University School of Medicine, the United States Public Health Service and others. The University of Wisconsin received over $60,000 under the committee on nutritional research. The work on aftereffects, carried on in many laboratories and hospitals, was made possible by grants totaling over $150,000, and the fields of epidemics and education were not neglected. Thus, a total of over $800,000 was used to combat poliomyelitis in 1941.

It is naturally impossible at this time to evaluate the results of the expenditure of such a large sum of money on the study of a single disease, particularly since many of the grants were for the continuation of studies that will not end for some years to come. One may say, however, that the work of the National Foundation for Infantile Paralysis in three years has profoundly affected present-day knowledge of the disease by making a broad and continuous attack on many fronts. New light has been thrown on the widespread nature of poliomyelitis, the problem of the healthy carrier, transmission of the disease by flies, the retention of the virus in sewage, the entrance of the virus into the body by various routes, the use of animals other than the monkeys for experimental purposes and new means of virus identification. In the field of aftereffects, the sponsoring of the investigations of Miss Elizabeth Kenny's technic of treatment has been outstanding. In view of previous criticism of this method, the decision of the foundation to investigate was not reached without long deliberation; however, the subsequent endorsement of the Kenny treatment by the Medical Advisory Committee is proof of the value of the foundation's farsighted policies. The educational needs have been met by grants for schools of nursing, scholarships, conferences and publications. Many field studies have been carried out by the Committee on Epidemics and Public Health. In general, material advances have been made, investigation has been stimulated and new knowledge has been added to the subject of poliomyelitis by the work of the foundation.

*The National Foundation for Infantile Paralysis, Incorporated: Annual report, 1941. Publication No. 38 of the Foundation. 58 pp. New York: National Foundation for Infantile Paralysis, Incorporated, 1941.

MEDICAL EPONYM

NÉLATON'S LINE

Professor Auguste Nélaton (1807–1873), surgeon of the Saint-Antoine Hospital, of Paris, called attention to this line in his *Éléments de Pathologie Chirurgicale* [*Elements of Surgical Pathology*] (Paris: Germer Baillière. 2: 441, 1847). A portion of the translation follows:

> If the exact relations of the great trochanter to the various bony prominences of the pelvis be examined in their normal state, it will be found that when the femur is flexed to a right angle and slightly adducted, the top of the great trochanter falls in a line that extends from the anterior superior spine of the ilium to the most prominent portion of the tuberosity of the ischium, and that this line divides the cotyloid cavity into two equal parts. This line, corresponding to the center of the cotyloid cavity . . . may easily serve as a guide to measure the degree of displacement [of the head of the femur]. . . . For this purpose, it suffices, after the thigh has been flexed to a right angle, to place a tape on the two points indicated, — that is, the anterior superior spine of the ilium and the ischial protuberance, — and to explore the gluteal region of both the sound and the injured side, to observe the difference between the two.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

TREASURER'S REPORT

COVERING REFUND DISTRIBUTION

The treasurer of the Massachusetts Medical Society makes the following report regarding the refund to district societies for 1942:

The Council voted to distribute the sum of $4000 to district societies. The total number of payments of annual dues received by the treasurer by March 4, to be counted for the refund, was 4023. Therefore the refund to the district societies for each paid fellow is $0.994.

The following table gives the number of payments as of March 1, and the refund to each district as of March 31:

DISTRICT	NUMBER REPORTED PAID	REFUND
Barnstable	41	$40.75
Berkshire	108	107.35
Bristol North	58	57.65
Bristol South	163	162.05
Essex North	180	178.95
Essex South	233	231.60
Franklin	36	35.82
Hampden	293	291.25
Hampshire	52	51.70
Middlesex East	123	122.26
Middlesex North	109	108.35
Middlesex South	779	774.33
Norfolk	697	693.82
Norfolk South	122	121.30
Plymouth	116	115.30
Suffolk	492	489.05
Worcester	346	343.92
Worcester North	75	74.55
Totals	4023	$4000.00

In 1941, for comparison, the total number of payments for the refund was 4038.

CHARLES S. BUTLER, M.D., *Treasurer.*

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: RETAINED PLACENTA FOLLOWED BY UTERINE AND TUBAL ABSCESSES AND DEATH

A seventeen-year-old primipara had had adequate care from the fourth month of pregnancy. Physical examination was negative, and the past history was irrelevant. Labor was complicated by a breech presentation, the labor itself being normal. The breech was delivered without difficulty. The baby weighed 6 pounds, lived only an hour, and showed numerous deformities, among them clubfeet, spina bifida and hydrocephalus. The placenta separated in part immediately because there was considerable hemorrhage, but it did not come away spontaneously. An hour after delivery, the patient was in shock. The placenta had not been obtained, and attempts to remove it were abandoned. During the night following delivery, there was more bleeding, the blood pressure falling to 80 systolic, 75 diastolic, with a pulse of 140. On the following morning, some fragments of placenta were obtained with a placental curette. A few hours later, the placenta was expelled spontaneously. Fifteen minutes after this, the patient had a chill, the temperature rising to 106°F. A high fever persisted until death, which occurred twenty-seven days later. The patient during this septic course was transfused twice and was given sulfanilamide. Autopsy showed an abscess of the right cornu of the uterus and of the right fallopian tube, with metastatic abscesses in both lungs.

Comment. This infection was probably due to attempts to remove the retained placenta, which may have been slightly adherent but was certainly not an accreta, as proved by autopsy. Autopsy also showed that the infection started in the uterus and became a blood-stream infection, with localized abscesses in the lungs. The sulfanilamide therapy was probably unintelligent. There was no evidence of uterine or blood culture on which to base this chemotherapy, but the patient was treated at the beginning of the era of chemotherapy, before proper standards had been established.

Retained placentas are inherently serious complications. So long as an adherent placenta or a retained placenta is unaccompanied by hemorrhage, it is wisest to leave it alone, often for as long as twenty-four hours — in the absence of bleeding — before manual attempts to remove it. Frequently, before the end of twenty-four hours, the placenta separates itself and is delivered spontaneously. In the presence of actual bleeding, the uterus must be invaded under the strictest asepsis. In no other way may a diagnosis be made and hemorrhage controlled. A retained placenta is easily removed, and a lightly adherent placenta may be manually separated from the uterine wall and removed intact. A placenta accreta can be diagnosed only by intrauterine examination. An accreta so diagnosed demands hysterectomy.

It is always wise to pack the uterus from which an adherent placenta has been manually removed. This is done for two reasons: to guard against subsequent hemorrhage; and to hasten the separation of small areas of placenta that have not been removed.

"THE CARE OF CRIPPLED CHILDREN"*

The Massachusetts Department of Public Health has recently completed its first five years of Services for Crippled Children. These services were made possible by a federal grant-in-aid authorized by the Social Security Act of 1935.

During this period, more than 2000 children who probably would not otherwise have been able to receive medical and surgical care and aftercare were admitted to the ten state-wide clinics that minister to crippled children. This service has cost a little over $400,000, including hospital care, so that the average expenditure for each child has been less than $200.

More than 600 of the 2000 crippled children who came to the clinics needed immediate surgical help, and were at once admitted to hospitals for operation. More than 150 had to have more than one operation. One had to be admitted to a hospital six times, and another child remained in the hospital continuously for twenty months.

These crippled children came largely from rural regions where there are few opportunities for them to receive the care they need. Even so, it is a matter of surprise that so many neglected crippled children actually were found because, as compared with other states, the Commonwealth is unusually well supplied with both public and private agencies that have for years been engaged in the humanitarian work of aiding the handicapped child. In administering this program, the department has been very careful to avoid supplanting the work of any of these agencies. The purpose of Services for Crippled Children has been solely, in the words of the Social Security Act, "to improve and extend existing services."

As a result of a study of what has been accomplished for crippled children by the Department of Public Health during the last five years, several interesting things have been learned.

AGE AND SEX OF CRIPPLED CHILDREN

More children come to clinic for the first time when they are in their sixteenth year than at any other age. If these adolescents came for help because of deformities caused by accidents or infections, one might conclude that they had been injured in their early teens, when children are on the streets more than when they are younger. But this is not so, for the great majority of patients at this age have had their disabilities for years.

The reason for not seeking aid sooner can only be inferred. That the age of sixteen is the most popular one at which to go to a clinic for help is particularly true of boys. Girls report in gradually increasing numbers beginning at the age of thirteen, through fourteen, fifteen and sixteen. One must conclude that many of the patients at the adolescent age, both boys and girls, come on their own initiative when they begin to take an interest in themselves and in their appearance. This change begins at a younger age in girls than in boys, and reaches its climax at sixteen in both boys and girls.

More than a third of all crippled children admitted to clinics came because of crippling conditions that they had had ever since birth. Most of these children were not seen until they were ten to fourteen years of age. However, the Department of Public Health has been offering this service for five years only, and many children had no opportunity to get aid earlier in life. Now that the clinics are more widely known and have achieved considerable reputation for excellent care, such children will probably apply for treatment at younger ages.

The reasons why parents do not bring their children to clinics at younger ages are several. They realize that treatment and apparatus are expensive, they fear the surgical operations that are so often necessary, and they think that the crippling condition is so hopeless that nothing can possibly be done to alleviate it. There are also, of course, those who believe that a deformity has been bestowed by the Deity and, therefore, should not be disturbed. On the other hand, certain parents will not regard a deformity as hopeless, no matter who has told them so, and go to every clinic and to every physician who can speak with authority, in the vain hope of finding someone who will promise physical restoration.

PROCEDURE FOR ADMISSION TO CLINICS

To be admitted to a clinic, a crippled child need only present an application signed by a physician licensed to practice medicine in the Commonwealth, preferably the family physician. A child thus admitted is given a thorough examination at the clinic, following which a complete social study of the patient's family is made by a public-health social worker. If this social study indicates that the child would be unable to obtain all the medical and surgical attention he needs without state or charitable aid, he is accepted for care. The information obtained by the social worker is also referred to the chairman of a special committee of the district medical society for an expression of his opinion concerning the child's eligibility for public care. Every effort is made to exclude from clinics all persons who are able to pay and who should pay for all the necessary treatment and apparatus. The final decision of eligibility for admission to a clinic rests with the Commissioner of Public Health. If patients can afford part of the services rendered, arrangements are made for them to pay the hospital or the brace maker.

PHYSICAL THERAPY

Many of the patients seen at the clinics do not require operations; they may need no other treatment than physical therapy. In such cases, the clinic consultant prescribes the treatment he wishes given, and arrangements are made for the physical therapist of that clinic district to visit the home periodically to carry out these recommendations. Where there are several patients in a community who require such treatment, they are brought together, if possible, at some convenient center and are there given treatment; the time of the physical therapist is thus conserved. Such an arrangement is not often possible, for most of the patients live in rural regions at some distance from each other. To have such patients brought to a central point would require transportation and the time of some other member of the family. The mother would generally not be able to take the time to go with the child, and thus one of the most important functions of the physical therapist would be lost — that of teaching the mother or an older sister what treatment to give and how to give it.

PREVIOUS MEDICAL AND SURGICAL CARE

Over 500 children had never had any medical or surgical treatment when they first came to a crippled-children's clinic. That such a situation existed in the Commonwealth has surprised those who insisted, before the Orthopedic Unit was organized, that few neglected children would be found. In all justice to the medical

*A "Green Lights to Health" broadcast given through Station WAAB by Dr. Edward G. Huber on Saturday, January 31, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

profession, it must be said that the reason for the neglect of these children was not that physicians had refused to help them but that the parents had made no effort to obtain care for their children. The tendency in some families is to hide the deformed child from other than members of the family, and thus to become so accustomed to the sight of the crippling condition that all thought of making the necessary efforts to correct the condition disappears.

Several hundred crippled children had had no other help before coming to the state clinic than the advice of their family physicians. It must be remembered that these children are a rural-dwelling group and that under such conditions the family physician's help is largely limited to giving advice, since he cannot afford to provide hospitalization or apparatus. The only hospitals ordinarily available to rural patients are the smaller ones, where free beds are not numerous and clinics are few. The Orthopedic Unit makes a particular effort to extend Services for Crippled Children to just such areas, to find and care for these children.

Over 300 of the clinic patients had had previous treatment in some metropolitan or local hospital. Practically all these children had had operative treatment, and this had nearly always been well done. But no matter how successful an operation, unless there is efficient aftercare and follow-up, much of the beneficial effect is lost. This was true in many of the patients seen in the clinics who had had operative procedures some years before admission, but who had had no aftercare. Many of them needed another operation, which might not have been necessary if they could have had good aftercare.

Many parents brought their children to the state clinic because they had found it necessary to discontinue the treatment their children were receiving, because of lack of sufficient funds. Treatment for crippled children generally extends over several years and expensive apparatus is frequently necessary.

More than 100 others discontinued their previous treatment because they had reached the age limit established by the agency under whose care they had been. Since patients are accepted at the clinic centers up to the age of twenty-one years, this is an excellent way to fulfill one of the purposes of Services for Crippled Children — to "extend existing services."

ACCEPTANCE OF RECOMMENDATIONS

The recommendations of clinic consultants are surprisingly well accepted. No special efforts are ever made to induce anyone to consent to operation. The risks and the possibility of unsatisfactory results, as well as the possible benefits to be derived from surgical interference, are explained to each patient's family. On the other hand, a parent's first refusal is rarely accepted as final, especially if there are good chances for improvement in that child's condition. The unco-operative patients are discharged from a clinic only after they finally and definitely refuse to accept aid, and after the clinic consultant and several members of the field staff have repeatedly talked with them.

Any patient who has been dropped from the active list because of refusal to accept the aid that has been offered may, of course, be readmitted at any time that the parent changes his mind and decides to accept aid. Occasionally, in flagrant cases of neglect, the Society for the Prevention of Cruelty to Children is called on for aid, which is gladly given. A child should not be penalized for life because ignorant parents refuse to allow him to have his handicap overcome.

It is remarkable that only a few have refused aid. This is a tribute to the clinic consultants and to the field workers, physiotherapists and social workers alike, who interpret the orthopedists' recommendations to the families. Most of the refusals came early in the program; they are rare now that the clinics have achieved a well-earned reputation for obtaining satisfactory results.

One cogent reason for this reputation lies in the continuity of the service offered, once the patients are accepted. They are examined by the clinic consultant, who is aided by the clinic supervisor, the physical therapist and the social worker. If physical therapy is prescribed, the patients see the same physical therapist again and again. The same social worker sees them repeatedly at their homes and in clinics. When they return to clinics, they see the same physician. If an apparatus is ordered, it is fitted by the physician, who gives full instructions concerning its use and who adjusts it as need arises. The physical therapist sees that the apparatus is properly used, makes any necessary adjustments if she can, or has the patient come to the clinic for this service. If an operation is recommended, the child is not merely turned over to a strange hospital staff. The clinic physician, whom the child knows, performs the operation. A very striking result of this careful, kindly follow-up care is the attitude of patients in the clinic sessions. A child on his first visit is often apprehensive and worried, and manifests his emotions by crying and by resisting the examinations. On subsequent visits, the contrast in the child's demeanor is striking, except in permanently unco-operative children, of whom there are fortunately not many.

Almost 1000 children are now under active clinic care, but there are still almost a hundred towns in the State, with a total population of about 160,000, from which no crippled child has yet been admitted to a state clinic. It is reasonable to assume that in many of these rural towns there are crippled children who are in need of care, and the Orthopedic Unit of the Department of Public Health plans to make special efforts to locate them so that they may be offered whatever help they need.

DEATHS

COOK — James H. Cook, M.D., of Quincy, died March 28. He was in his fifty-ninth year.

A native of Newcastle, Maine, he received his degree from Tufts College Medical School in 1910. He was a fellow of the American College of Surgeons and a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son, two brothers and a sister survive him.

FREUND — Ernest Freund, M.D., of Boston, died recently. He was in his sixty-fifth year.

Dr. Freund received his degree from the Medical Faculty of the University of Prague. He was a member of the Massachusetts Medical Society and the American Medical Association.

MELEDY — Joseph A. Meledy, M.D., formerly of Milton, died April 1. He was in his fifty-first year.

Dr. Meledy received his degree from Tufts College Medical School in 1918. He was for many years a physician in the regional office of the Veterans Administration in Boston. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1942

Diseases	February 1942	February 1941	Five-Year Average*
Anterior poliomyelitis	2	0	0
Chicken pox	1651	1103	1440
Diphtheria	11	6	12
Dog bite	489	531	568
Dysentery, bacillary	3	12	17
German measles	261	89	74
Gonorrhea	326	282	346
Measles	1755	1896	2244
Meningitis, meningococcal	13	6	8
Meningitis, other forms	13	†	†
Mumps	1930	696	740
Paratyphoid infections	4	4	2
Pneumonia, lobar	478	461	628
Scarlet fever	1399	528	828
Syphilis	374	344	413
Tuberculosis, pulmonary	240	176	179
Tuberculosis, other forms	14	12	19
Typhoid fever	6	3	4
Undulant fever	5	5	3
Whooping cough	780	930	952

*Based on figures for preceding five years.
†*Meningitis, Other Forms* (except Pfeiffer Bacillus) not reportable until May 13, 1941.

Geographical Distribution of Certain Diseases

Anterior poliomyelitis was reported from: Amherst, 1; Boston, 1; total, 2.

Diphtheria was reported from: Cambridge, 1; Everett, 1; Framingham, 1; Lowell, 3; Somerville, 1; Springfield, 1; Waltham, 1; Wilbraham, 1; Worcester, 1; total, 11.

Dysentery was reported from: Tewksbury (State Infirmary), 3; total, 3.

Malaria was reported from: Fort Banks, 1; total, 1.

Meningitis, meningococcal, was reported from: Ayer, 1; Braintree, 1; Brockton, 1; Fall River, 1; Fitchburg, 1; Gloucester, 1; Greenfield, 1; Melrose, 1; New Bedford, 2; Reading, 1; Waltham, 1; Weymouth, 1; total, 13.

Meningitis, other forms, was reported from: Barre, 1; Boston, 3; Brookline, 1; Easton, 1; Fitchburg, 1; Grafton, 1; Marshfield, 1; North Reading, 1; Springfield, 1; Sturbridge, 1; Worcester, 1; total, 13.

Paratyphoid infections were reported from: Boston, 1; Gardner, 2; Quincy, 1; total, 4.

Pellagra was reported from: Boston, 1; total, 1.

Septic sore throat was reported from: Amesbury, 1; Boston, 3; Brockton, 2; Cambridge, 1; Chelmsford, 1; Georgetown, 1; Greenfield, 1; Ipswich, 1; Malden, 2; Merrimac, 1; Newton, 1; Northbridge, 1; Salem, 1; Winchendon, 2; total, 19.

Typhoid fever was reported from: Boston, 3; Lowell, 1; Stoughton, 1; Worcester, 1; total, 6.

Undulant fever was reported from: Ashburnham, 1; Brookfield, 1; Lee, 1; Millbury, 1; Weymouth, 1; total, 5.

Mumps, after showing record-high incidence for the past seven consecutive months, is still at a high level.

Chicken pox, meningococcal meningitis, German measles, poliomyelitis, paratyphoid, scarlet fever, pulmonary tuberculosis and undulant fever were reported at figures above their five-year averages.

Bacillary dysentery, measles, lobar pneumonia, other forms of tuberculosis and whooping cough were reported at figures below their five-year averages.

The focus of animal rabies previously noted in the northeastern section of the State is still active in Middlesex County. Cases were reported from Tewksbury, Lowell and Woburn.

NOTES

George R. Cowgill, associate professor of physiological chemistry at Yale University and editor of the *Journal of Nutrition*, was recently awarded the $1000 Mead Johnson and Company prize by the American Institute of Nutrition for researches dealing with the vitamin B complex. The presentation was made to Professor Cowgill by Dr. Albert G. Hogan, professor of agricultural chemistry at the University of Missouri and president of the Institute, at exercises in The Copley-Plaza, Boston.

Dr. Richard P. Strong, professor emeritus of tropical medicine at Harvard Medical School, recently delivered the fifth series of the John Wyckoff Lectures at New York University College of Medicine. The general title was "Tropical Diseases and the War," and at the first lecture, Dr. Strong discussed dysentery, typhus fever and plague, and at the second, trypanosomiasis and onchocerciasis.

CORRESPONDENCE

DIPHTHERIA ANTITOXIN

To the Editor: The Department of Public Health has been distributing diphtheria antitoxin in packages of 1000, 5000 and 10,000 units. Since present opinion favors the administration of at least 10,000 units to all but the very mildest cases of the disease, the department is discontinuing the distribution of the 5000-unit package. When it is desired that only 5000 units be administered, the appropriate amount may be obtained from a 10,000-unit package.

The elimination of this package will also effect economies in the use of paper and glassware, both of which are becoming increasingly difficult to obtain. Because of this increasing scarcity, the department likewise earnestly requests the co-operation of physicians, hospitals and boards of health in the maintenance of all possible economies in the distribution of biologic products. By ordering only the quantities needed for two to four weeks, and by promptly returning all unnecessary surplus stocks, outdated products and empty containers, the department will be greatly aided both in maintaining an adequate supply of needed materials and in effecting economies in the distribution of biologic products. Materials to be returned should be sent to the Antitoxin and Vaccine Laboratory, 375 South Street, Jamaica Plain, Massachusetts.

Paul J. Jakmauh, M.D.
Commissioner of Public Health
State House
Boston

REPORTS OF MEETINGS

BOSTON ORTHOPEDIC CLUB

A regular meeting of the Boston Orthopedic Club was held at the Boston Medical Library on November 17. Colonel Norman T. Kirk, of Washington, D. C., spoke on "The Evacuation and Emergency Treatment of War Wounded." A tentative plan for the management of wounded in a zone of advance includes an aid station for each battalion, a collecting hospital for these stations, a clearing hospital and an evacuation hospital. The first of these can naturally be employed only when the position of the troops is established, not in advance or retreat. There should be medical troops with each battalion, and

minimal medical equipment consists essentially of first-aid material. Their function is the carrying of the wounded to the collecting station, at which point the task of the medical regiment ends. Thereafter, it becomes the duty of the army to transport the patients.

The progress through the various stations of a hypothetical patient with a compound fracture of the femur was traced. Since all soldiers now receive three prophylactic injections of tetanus toxoid, the administration of tetanus antitoxin is no longer a problem for the first-aid station. The first-aid pack that each soldier carries contains 90 gr. of sulfanilamide, with instructions for its use in compound fractures. Iodine is used around the wound immediately, and an occlusive dressing is applied. A Thomas splint is applied, but no ankle hitch is employed because of the danger of trauma if a long haul is necessary. Blankets are wrapped in a manner designed to lessen the degree of shock. Morphine is administered either on the litter or at the aid station. Sulfanilamide is given orally in doses of 15 gr. every four hours until discontinued at some later post; its later use in the wound itself is a matter of choice at these centers. Sodium amytal, which has been demonstrated to decrease the degree of surgical shock, may be employed in the future. It has been estimated that proper splinting diminishes the shock of original transit from 50 to 15 per cent. There is not much specific shock therapy at the aid station, except the use of blankets, for heat, and of the Trendelenburg position.

The collecting station is about 1000 yards behind the aid station, and transportation between these points is accomplished by litter only. It has been shown that to traverse such a distance under war conditions of shell fire requires from one to two hours. At this point, there is also very little protection or specific treatment, but some segregation of patients can be carried out.

Transportation from here to the clearing hospital, three or four miles away, is accomplished by ambulances and requires an hour or more. Advancing troops always have the right of way on the roads and may seriously hamper the evacuation of wounded. Furthermore, there is no ambulance service by day unless air supremacy is certain, and patients may thus be forced to wait over in the meager collecting hospitals for as long as eighteen to twenty-four hours. At the clearing hospital, which consists merely of tents, the cases are divided and allocated to their appropriate places. Here also, the first bit of secondary treatment is carried out, such as the repair of splints and the renewal of dressings. Plasma or serum is administered to patients in extreme shock. An emergency surgical unit associated with this clearing hospital takes care of urgent abdominal, thoracic and head injuries, as well as bleeding cases. Amputations are performed on cases that would otherwise be nontransportable. Unfortunately, no operative case can be transferred for six days, which is much too long if a retreat becomes necessary. Airplane ambulances are desirable and feasible, but can be supplied only after fighters, bombers and transport ships have been made available in sufficient numbers. No intricate apparatus is employed to evaluate the shock of a patient, but clinical diagnosis is relied on.

The wounded are then taken by the army ambulance corps to an evacuation hospital ten to twenty miles in the rear. It was pointed out that, because of the rapid change of battlefield, trucks rather than trains may become a necessity for the carrying of supplies for such centers in the rear. Each of these hospitals usually has about 750 beds, but as many as 2500 cases may be referred to it during a twenty-four-hour period. Segregation of the more urgent is, therefore, again necessary. The hypothetical fractured femur is still on the original litter and fixed in the same Thomas splint. Depending on the severity of the injury and the amount of congestion at the hospital, the fracture may be repaired at this point. For mechanical cleansing, there will undoubtedly not be enough water and saline to carry out the desired technic. Therefore, mechanical cleansing takes the form of cutting away all devitalized tissue and removing foreign bodies and bone fragments. Here, for the first time, dried blood and plasma are available for all. More emphasis is being placed on the thorough treatment of "simple" wounds at this hospital, with the idea of retaining the soldier in the battle area and thus not losing him for the duration so far as that sector is concerned. These wounds are débrided carefully, dusted with sulfanilamide and primarily sutured. Formerly, many such soldiers would either have succumbed to gas-bacillus infection or have been lost to their company. This latter fact was considered bad for the morale.

The further treatment of compound fractures is by the Orr method, which comprises the thorough cleaning and débriding of the wound and the immediate application of plaster after the wound has been packed with an impregnated gauze. It is reported that in the recent Spanish war there was only one death from gas infection in over a thousand cases, and that only eight casts were removed because of sepsis. Dr. Kirk offered the objection that most of the patients with gas-bacillus infection would have been dead before arrival at this station. Furthermore, the treatment of fractures by this method affords only mediocre results at best, and is not recommended for fractures of the femur. There is evidence that there may be considerable collections of purulent material in joints and soft tissues despite the absence of fever or pain, and this leads to cachexia and chronic debility. It has been concluded by the French observers, therefore, that such treatment of compound fractures is advisable only for short hauls. On the whole, Dr. Kirk believes that plaster is not effective in the stabilization of fractures of the shafts of long bones. Matthews, of London, does not dare use plaster even for short journeys without splitting the cast or making a window, either of which defeats the purpose of this method. Even its staunchest advocates do not use this technic if there is any soft-tissue damage, and insist on twenty-four hours of observation before transportation. Some surgeons strongly advocate the use of sulfanilamide locally, whereas others use only vaseline packs. Dr. Kirk favors the use of 10 gm. of sulfanilamide locally, packing of the wound, fixation by a Thomas splint or skeletal traction and the continuance of chemotherapy orally. A wound is considered potentially clean only if it is widely débrided and loosely packed.

Statistics reveal that 30 per cent of all injuries are associated with compound fractures — 6 to 8 per cent of an infantry division become casualties in each day's fighting, the proportion of killed to wounded being 1:4. Therefore, the number of casualties daily is 900 to 1000 men for each division.

The discussion was opened by Dr. Elliott C. Cutler, who advocated the blood grouping of all soldiers and their congregation in companies according to such groupings. The expert training of the members of the aid station was highly recommended, since this is often the place where the most important dressings are carried out. Time is most vital in abdominal injuries, and in thoracic wounds and head injuries. The last are apparently decreasing with the diminishing use of trucks in actual

warfare. It was warned that many more wounded will of necessity be left in the field with the increasing mobility of war, for they cannot be transported fast or far enough with trucks. The use of plaster, for transportation only, was urged as a means of comfortable and easy removal. It was pointed out that chloroform is an ideal anesthetic for healthy young men: it has a rapid induction and recovery, is of small bulk, and is good in the desert or on shipboard.

Dr. G. W. Taylor stated that intravenous anesthesia may be the answer to that problem, at least partially. He expressed some dissatisfaction with the reported results of the Orr method of treating compound fractures.

Dr. R. C. Cochrane believes that splints give good immobilization, with a minimal amount of shock. Although army regulations are admittedly necessary in the front hospitals, some allowance for variation in technic should be made in the evacuation and general hospitals. Plaster as a means of immobilization for short hauls may be acceptable, but it becomes particularly dangerous for any prolonged period because of the lack of signs and symptoms in the event of sepsis.

Dr. O. J. Hermann read excerpts from letters of Dr. Charles Bradford, in England, which indicate that the Orr method is gaining wide acceptance even among men who saw and used other methods, but that it is not used blindly in every case. For the treatment of shock, strategically placed stations permit rapid delivery of all types of blood. There has been some trouble with the coagulants in plasma. Serum has proved effective, especially in the initial treatment of burns. For anesthesia, nitrous oxide, oxygen and ether and chloroform are still being widely used. Nitrous oxide is good for chest surgery, especially in avoiding complications. Pentothal may supplant some of these for shorter procedures.

In conclusion, Dr. Kirk stated that although chloroform is a good, safe anesthetic in competent hands, there are not enough such trained men. Nitrous oxide, oxygen and ether is being used in Egypt with great success. Plasma has been used extensively at the Walter Reed Hospital, with no reactions. The Roger-Anderson method for the treatment of fractures has fallen into disuse in the army because of the incidence of osteomyelitis and the failure to control the pain adequately. Furthermore, there is not the free motion at the joint that is so widely publicized, for the fixation pushes the surfaces together.

UNITED STATES NAVAL HOSPITAL

At a regular meeting at the United States Naval Hospital in Chelsea on January 9, Dr. Francis T. Hunter, recently of the Massachusetts General Hospital and now a member of the Medical Corps of the United States Naval Reserve, spoke on "Transfusions." The discussion was confined to some of the difficulties with and the new developments in the use of blood and its substitutes. Dr. Hunter added that the Army and Navy are now typing the blood of all men in the armed forces and attaching an identification tag with this information to each individual, the Landsteiner method of nomenclature being employed.

Some of the possibilities of blood typing in legal medicine were pointed out. If one parent is Group AB and the other is Group O, all the children will be either Group A or B. Another corollary of this rule is that if either parent is Group AB, there can never be any children with Group O. Infants can be typed immediately after birth, for the agglutinogens of the human cells are present early in fetal life; however, the agglutinins of the serum may not be detectable for several months or even a year, so that infants may occasionally receive blood of other types without mishap. Subgroups 1 and 2 of Group A are often blamed for reactions and deaths, but there is as yet no good evidence that they are clinically significant. All groups have Subgroups, m, n or mn, which seem to be unimportant for transfusion purposes but may help in medicolegal problems.

Since the agglutinins of serum are destroyed by bacterial contamination, test serums should be discarded after one week. One should also be careful of the cleanliness and the type of glassware, since serum deteriorates in the presence of alkali. If test serum is being made by an institution, care should be taken to titrate the serum before pooling, and only high-titer serums should be employed — otherwise, incompatibilities may not be detected in typings. Lecithin has proved a valuable aid in ruling out pseudoagglutinations due to rouleaux formation. By placing a small amount of this substance, which increases the surface tension of the cells and prevents the formation of biconcave disks on the slide, rouleaux formation is avoided. This occurs primarily in acute infections or in any person with an increased sedimentation rate. If any doubt of the compatibility of donor and recipient of the same type remains after all the usual measures have been tried, 20 cc. of blood from the donor may be injected into the recipient; the rest of the transfusion can be safely given if there is no reaction within twenty minutes.

It is reported that, when all known causes of transfusion reactions have been removed, there are still slight temperature elevations in from 25 to 50 per cent of recipients. But if the blood is taken when the donor is fasting, these slight febrile reactions are reduced to about 3 per cent; furthermore, this results in a much smaller number of other allergic reactions. Reactions from unclean apparatus are now rather a minor consideration. One final warning is for the person taking the blood to make sure that the donor is who he is supposed to be, for such errors have led to lawsuits.

Dr. Hunter then discussed blood banks and blood substitutes. The former are expensive and troublesome, but are of value in communities where there is no supply of readily available donors. Even when refrigerated, whole blood changes with time and especially under conditions that increase the number of enzymes. All these factors favor laking of the erythrocytes, and free hemoglobin in the circulating blood causes changes of the renal tubules, that may be fatal — incidentally, these changes are similar to those of arsine gas poisoning, which apparently causes laking of the circulating erythrocytes. Agitation also lakes red blood cells, and this factor has made traveling blood banks for armed forces impracticable. The best blood bank is that provided by the men in service, with type tags attached, in whom the freshness of the blood is ensured.

Plasma will never completely replace whole blood, for erythrocytes are eventually necessary in most cases. It is better than whole blood in burns, because of the hemoconcentration, but has not proved so beneficial in nephrosis as had been hoped. Liquid plasma obtained from the deteriorating blood of blood banks apparently lasts only about nine months, whereas dried plasma seems to stay unchanged for as long as five years. The latter product is now available on the market for $26.22 for the equivalent of 250 cc. of liquid plasma, which is equal in osmotic effect to a 500-cc. whole-blood transfusion and is therefore not very expensive. The beef albumin of

Cohn appears very promising; he has already removed the beef antigens and is rapidly finding methods for removing other impurities. This may be a cheap blood substitute and may outmode all others as a temporary expedient. This is another argument against investing large amounts of money in blood banks at the present time.

The following points were brought out by Dr. Hunter in the discussion. Although it may be possible to use Group O donors with impunity, in many cases, occasionally in recipients who have had either no previous transfusions or one from another type, it is not wise to give multiple transfusions from a so-called "universal donor"; for, in certain cases, there may be a temporary heightening of the agglutinin titer and a true and serious reaction of incompatibility. If one must employ this type, it is advisable to take serum for direct matching from the recipient between each transfusion.

The early and unmistakable signs of kidney shutdown from an incompatible transfusion reaction are renal pain, cyanosis, chest pain and dyspnea. These occur almost immediately, and reactions after three or four hours are usually attributable to some foreign protein from the apparatus or donor. Decapsulation for renal failure will probably not prove efficacious, if the experience at the Massachusetts General Hospital is any criterion, for it has been shown that such a kidney puts out less urine than its nondecapsulated mate. Alkalinization of such patients is logical, for hemoglobin is more soluble at a higher pH. This will probably not result in the solution of crystalline material, in the kidney tubules, but may prevent the further precipitation of hemoglobin.

BOOK REVIEWS

Diseases of the Nails. By V. Pardo-Castello, M.D. With a foreword by Howard Fox, M.D. Second edition. 8°, cloth, 193 pp., with 94 illustrations. Springfield, Illinois: Charles C Thomas, 1941. $3.50.

The manifestations of disease in the nails are puzzling to most physicians. This book should therefore be a welcome addition to any medical library, whether of the individual physician or of the medical school or hospital.

The text of this edition has been definitely improved. Emphasis has been placed on the numerous general diseased conditions in which nail changes may occur, as well as on affections peculiar to the nails. The histology and pathology are discussed rather briefly, but an excellent feature of the book lies in the many and excellent photographs, which aid so much in the assimilation of the text. Attention should be called to two valuable tables — one regarding the occupations with characteristic nail changes and the other listing changes caused by poisons. An extensive bibliography and numerous excellent illustrations add much to the value of this book.

Teaching Preventive Medicine to Medical Students, with Special Reference to the Use of Health Department Facilities. By Hugh R. Leavell, M.D., D.P.H. 8°, paper, 77 pp., with 9 tables. New York: The Commonwealth Fund, 1941. 25c.

A discussion of the use of health-department facilities for teaching preventive medicine to medical students is timely, since this is one of the more recent suggestions in the field of public health, and one that has already been tried out in many medical schools. The material reported was gathered by the questionnaire method, and has been sifted by an author who is obviously familiar with the difficulties faced by both medical schools and health departments. It is of particular interest to those concerned with this phase of medical education, and has many tables and comments that may be of interest to others. It is a carefully prepared and worth-while statement of the subject for 1941, and one hopes that a comparable study in 1951 not only will be made but will show a natural growth of this potentially valuable method of instruction.

The Therapeutics of Internal Diseases. Supervising editor: George Blumer, M.D. Associate editor: Albert J. Sullivan, M.D. Three volumes. 8°, cloth. Vol. I: 872 pp., 136 illustrations, with 26 tables and 1 chart. Vol. II: 1042 pp., with 2 charts and 14 tables. Vol. III: 738 pp., 39 illustrations, with 1 chart and 2 tables. New York: D. Appleton-Century Company, 1941. Sold only as a set, $40.00.

In these days, when the literature on any detail of medicine has become so voluminous, it is impossible for any physician to make inquiry with satisfaction among the many interesting, scattered findings and advances in the field of therapeutics. Indeed, the literature increases so rapidly over the field as a whole that one is forced to retreat in blind confusion. To overcome this situation, compilations of data known as reference books are published. Even if a penitential search through a series of reference works consumes time, it remains, so far, the most satisfactory method of obtaining information of various kinds from competent authority. Further elaboration can be pursued from reference minutiae.

With this in mind, one can consider the worthy enterprise edited by George Blumer. Volume I contains the following splendid sections on "Nutrition and Dietetics" (A. Smith); "The Principles of Endocrine Therapy" (K. W. Thompson); "The Principles of Serum and Vaccine Therapy" (M. Eaton); and "Specific Therapeutic Technics" (W. J. Bruckner). Unfortunately, this helpful material is sandwiched among some four hundred pages of questionable therapeutic procedures from spa therapy through a galaxy of peculiar methods of various forms of physical therapy. This section on physical methods is muddled and poorly planned, and merely adds to the confusion already present in physical therapy, emphasizing its lack of physiologic background.

Perhaps the most important and best presented section is in Volume II. The four hundred and fifty-four pages dealing with pharmacology, therapeutics and toxicology, written by Louis S. Goodman, stand well above the rest of the sections and form the bulwark for the entire edition. The section on virus diseases (J. R. Paul, G. Klatskin and M. E. Howard) is a dried extract withdrawn from already present standard reference material and reveals the stigmas of resemblance with some face lifting to other compilations. Thus, this section, which should be of great interest today, reveals none of the remarkable interrelations among virus diseases. In the same volume, the sections on Rickettsiae (Blumer), and more especially the mycobacterioses (E. N. Packard, H. E. Hasseltine and W. T. Longcope), the bacillary infections (J. H. Musser and P. H. Jones, Jr.), and the coccal infections (M. Finland, C. S. Keefer and E. H. Place) are superb analyses and dissertations.

Volume III includes a chapter on diseases due to fungi (D. T. Smith), a remarkably capable section by Faust on metazoan diseases and, no less interesting, a precise chapter by Craig on protozoan diseases. These sections show careful review and study and include material on intoxications (Blumer). The section on diseases of physical

agents is incomplete, and the authors (E. Lawrence and H. Martland) fail to elucidate from a physiologic standpoint the nature and treatment of accidental electrical injuries. Seasickness is not linked up with any of the important work done in Britain on this subject. However, this part of the volume is offset by reliable sections on the treatment of diseases of the lower respiratory tract (D. S. King), the treatment of diseases of the blood and lymph vessels (I. S. Wright), and the treatment of heart disease and heart failure (H. M. Marvin).

On the whole, the three volumes represent the time-consuming editorial efforts of Dr. Blumer, who with great care has attempted to assemble data pertinent to therapeutics; indeed, it is today the best of its kind for its comprehensive scope.

Observations Made during the Epidemic of Measles on the Faroe Islands in the Year 1846. By Peter L. Panum, M.D. 8°, cloth, 111 pp. New York: published by the Delta Omega Society and distributed by the American Public Health Association, 1940. $2.50.

In the year 1846, an epidemic of measles in the Faroe Islands offered an exceptional opportunity for the study of the disease. The population was scattered, sparse and virtually nonimmune, since measles had not appeared there for sixty-five years. Moreover, no other eruptive fever was present to confuse the issue. The conditions possessed "the potentialities of a vast experiment." But successful experiments require sharp observations, imagination and an open mind. These Panum had; and the man and the occasion met. The result is one of the classics of epidemiology.

Up to this time, as Dr. Doull points out in his introduction, it was still believed that, although measles was usually spread by direct contact, it might sometimes arise spontaneously, and the notion of a *contagium vivum* as the cause was held by very few. It was supposed that the disease was most readily transmissible in the desquamative stage, and estimations of the incubation period varied widely.

Panum settled the fact once and for all that the exanthem appeared with great regularity thirteen or fourteen days from the effective exposure, which meant that the disease was transmitted "at precisely the time that the exanthem was breaking out or had just broken out." He said nothing of infectivity prior to the eruption, although some of his histories indicated it. He doubted, if he could not prove, that the disease was not transferable in the posteruptive period. He himself observed no instance of transmission by fomites. He offered, it is true, no explanation of how the infectious material is passed out of the body; indeed, he hazarded no opinion concerning the nature of the morbific agent. Regarding spontaneous origin, he could only say that it did not occur in the Faroe Islands. Nevertheless, his work will stand for all time, and it is most fitting that it should be published in this handy translation.

The Pharmacology of Anesthetic Drugs: A syllabus for students and clinicians. By John Adriani, M.D. Second edition. 4°, cloth, 86 pp., with 102 illustrations. Springfield, Illinois: Charles C Thomas, 1941. $3.50.

There has always been a real need for a book of this type, which correlates clinical anesthesia with the pharmacology and physiology of the drugs in current use, for both the clinician and the medical student. Indeed, it is a book well worth reading to refresh one's mind on the action of the lethal drugs used outside the field of anesthesia.

The author has accumulated his data from numerous observations and personal experiments. The material is presented in an honest, scientific manner, with the thought that the facts presented might serve as a guide until further investigation may be obtained. The subject matter is uniquely arranged in diagrammatic fashion, to focus attention on the physiologic and pharmacologic changes occurring with the various organs and systems of the human body, so that further study and interest in the fundamental sciences associated with anesthesiology may be stimulated.

The subjects covered include general properties and chemical natures of anesthetic drugs, general systemic effects on the respiratory, circulatory and central nervous systems, and disturbances of respiration including oxygen and carbon dioxide transport, oxygen want and the physiology and toxic effects of carbon dioxide.

The various anesthetics include gaseous agents (nitrous oxide, ethylene and cyclopropane), volatile agents (ethyl ether, divinyl oxide, chloroform and ethyl chloride), nonvolatile agents (bromethanol with amylene hydrate [Avertin], trichlorethanal and paraldehyde), barbiturates, local anesthetics and opiates. The nonanesthetic drugs used in conjunction with anesthesia are also discussed. In the last chapter, some clinical considerations are presented, such as preanesthetic medication, technics of administration, carbon dioxide absorption, complications and accidents, anesthetic and respiratory complications, and the explosibility of anesthetics. There is also a brief bibliography, which covers more recent contributions to this field of medicine.

Clinical and Experimental Investigations on the Genital Functions and Their Hormonal Regulation. By Bernhard Zondek. 8°, cloth, 264 pp., with 59 illustrations and 44 tables. Baltimore: Williams and Wilkins Company, 1941. $4.50.

Many of the advances in knowledge of the sex hormones are associated with the name of Zondek. The author includes in this short monograph a résumé of his lifework with sex hormonology, as well as a review of the work by other investigators that corroborates his findings. This volume is of monumental scope, and bears witness to his intense pursuit of facts. Typical of the pure scientist are his experiments with water from the Dead Sea. All layers of the sea were analyzed, and it was found that the water and sludge at the bottom contain large amounts of estrogenic substances, whereas other layers have little or none.

The chapter entitled "Fate of Sex Hormones in the Organism" shows that naturally occurring estrogens are rapidly destroyed in the body, whereas synthetic estrogens (Stilbestrol) are very slowly destroyed. This accounts, perhaps, for the powerful and often toxic action of the latter. Evidence is presented to show that the corpus-luteum hormone can produce bleeding of the uterine mucosa alone, whereas it had been supposed that this was possible only in a mucosa previously prepared by the action of estrone. On the basis of present knowledge, an interesting and plausible theory for the menstrual cycle is advanced.

Many of the facts presented in this volume will form the basis of future clinical experiments. The book makes interesting reading for both the practitioner and the investigator, because the author deals throughout with clinical and animal experiments.